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BUREAU OF HYGIENE AND TROPICAL DISEASES.

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SUMMARY OF RECENT ABSTRACTS.*

VIII. TYPHUS GROUP OF FEVERS.

Proteus OX19 type. Vectors: louse and flea.

IONESCO-MIHAESTI *et al.* (p. 255) report a serious outbreak of typhus in Bessarabia in 1936-37, and indicate the preventive measures taken, which included isolation of cases and mass delousing of the general population. BARLOVATZ (p. 565) describes louse-borne typhus in the forest region of the Congo, giving clinical details; *Proteus OX19* and *OXK* are agglutinated in high titre. Children are seldom ill and mild cases may be mistaken for influenza, dengue or paratyphoid; many of the natives appear to be immune. In the wards bed-to-bed infection is rare, but most of the imported ward personnel were attacked. CLEAVE (p. 257) reports two cases of the *Proteus OX19* type in Hong Kong.

CASTANEDA and SILVA (p. 259) recognize three types of typhus in Mexico: murine, intermediate and the historic type, though there was no epidemic of the last about the time when the investigations were made.

KUCZYNSKI-GODARD (p. 564) describes "micro-epidemics" of typhus in the Peruvian highlands. In silent areas Rickettsia-infected lice have been found on the inhabitants, though no cases of typhus have been seen, and there is no evidence of Rickettsia other than those of typhus. It is thought that non-immune people coming into contact with apparently healthy carriers of infected lice give origin to the micro-epidemics.

MACCHIAVELLO (p. 255) found that after centrifugation of emulsions of tissues containing *R. prowazeki* the intensity of disease set up by injection of the supernatant fluid varies according to the number of Rickettsiae left in the fluid, and that if all the Rickettsiae are removed, the fluid no longer gives rise to the disease.

BLANC and BALTAZARD (p. 573) lay down criteria required for the proof that a typhus virus is adapted to a particular insect host. They

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1940, Vol. 37. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

have found that the virus of epidemic typhus can satisfy these requirements in the flea *Xenopsylla cheopis* [and presumably, therefore, may be transmitted by this flea].

Macchiavello (p. 256) describes a new method of staining Rickettsiae.

Joannon Infante (p. 258) describes a rapid microtest for typhus in which blood from a finger is used for agglutination of an emulsion of *Proteus X19*. There is apparently close agreement between this test and the full Weil-Felix reaction.

Danielopolu and Craciun (p. 566) show that in severe typhus there is an increase in the number of red blood cells, and a leucocytosis due to an increase in the mononuclear cells. Typhus nodules are caused by toxic desquamation and multiplication of the endothelial lining of the capillaries. Plasmocytes may be seen in blood films and their presence is a point in differentiation from typhoid. Danielopolu *et al.* (p. 567) consider that the nervous symptoms of typhus are due, not to toxic action on the nervous system, but to lesions in the capillaries of that system. The cerebrospinal fluid becomes yellow owing to the presence in it of altered blood pigments. They discuss the differential diagnosis from typhoid and relapsing fever, and the methods of prophylaxis, including vaccination, which should be employed. Le Renard and Raynaud (p. 258) describe a case of toxic nephritis in typhus, which was relieved by decapsulation of one kidney ; they regard the nervous symptoms of typhus as due largely to toxic nephritis.

d'Ignazio *et al.* (p. 565) describe polyneuritis, with permanent damage, as a sequela of typhus in Abyssinia.

Giunta and d'Ignazio (p. 257) treat their patients according to the analogies they present with scurvy and beriberi, giving ascorbic acid and vitamin B by injection. Pressure in the cerebrospinal fluid is relieved by lumbar puncture. Masucci (p. 257) discusses the treatment of typhus. Convalescent serum may be used, with subcutaneous saline or glucose for the toxaemia, and cardiac stimulants and bromides.

De la Rivière (p. 570) gives a clear account of preventive measures to be taken in connexion with louse-borne typhus. General measures consist of supervision of populations, their movements and their standards of personal cleanliness. The layout of special typhus hospitals is discussed, together with methods of delousing by disinfection and by close cutting of scalp and body hair. Louse-proof clothing for workers is referred to and mention is made of prophylactic vaccination. Nicolesco (p. 571) discusses the protection of medical workers by means of louse-proof clothing and vaccination. Mühlens (p. 571) writes of preventive measures taken during the war of 1914–1918 in Bulgaria and Turkey.

Ruge (p. 259) records a case of ship typhus, with agglutination of *Proteus OX2* but not *OX19*, in Hamburg. Rats captured in the docks gave positive Weil-Felix reactions in 1933, but the author considers, in this instance, that infected rats may have boarded the ship on which the patient was found, when it touched at a Spanish Mediterranean port. Reitler *et al.* (p. 259) describe endemic typhus as seen in Palestine, where it is usually a disease of non-immunized immigrants. Two types are distinguished, in both of which *Proteus X19* is agglutinated, the one moderately severe, the other

very severe. CELIK (p. 841) notes that in Istanbul certain cases of typhus (presumably murine) show strong reactions with *Proteus OXL* rather than with *OX19*, thus resembling the Lima type.

MAISTER *et al.* (p. 260) have isolated strains of murine virus from rats, fleas and from one human patient employed in a grain store in Natal, S. Africa; this is the first time this virus has been isolated there, but cases of flea-borne typhus have probably occurred before.

Cases of typhus, with positive reactions to *Proteus OX19*, are reported from Bombay by PATEL (p. 840) and from Bangalore by SHARMA (p. 840). In many the provisional diagnosis of typhoid had been made until negative Widal and positive Weil-Felix reactions revealed the true nature of the disease. The vector is probably the rat flea. WOLFF (p. 261) isolated a murine strain from rat fleas from the house of a typhus patient in Ceylon.

WOLFF and DE GRAAF (p. 262) state that shop typhus [the murine form] in which the serum agglutinates *Proteus OX19* is not uncommon in Java. Agglutinins appear late, however, and for blood to be infective for animals it must be taken during the period of fever. The scrotal reaction is produced in guineapigs, and the authors point out that similar reactions may be given by *Spirillum minus* and *Pfeifferella whitmori*, though there are certain differences. The *Proteus OXK* type of typhus virus does not give the scrotal reaction so frequently as the murine type.

RAYNAL *et al.* (p. 256) record an outbreak of 1,000 cases of murine typhus in Shanghai in 1938, but consider that this disease was transmitted from man to man by the louse. The strains isolated from man appear to be intermediate between the murine and the classical human types and this indicates that the murine type, escaping from the rat-flea-rat cycle, can attempt adaptation to the man-louse-man cycle, achieving *en route* various stages which mark its progress towards a historic typhus virus. In this connexion the finding of SPARROW (p. 267), that murine virus can multiply abundantly in the intestine of the louse, is noteworthy. RAYNAL (p. 569) further states that though *Ctenocephalus musculi* were found on infected rats, no virus could be isolated from them. No fleas of the genus Xenopsylla could be found.

LIU and CHUNG (p. 261) have isolated murine strains from man, rats and fleas in Peiping.

In North America endemic typhus has recently spread more and more from the coast of the Southern States into rural areas, and for this DYER (p. 571) suggests two reasons: mass rat migrations due to increased cultivation of food crops in place of cotton, and the fact that field mice have been found infected in nature. BOWDOIN and BOSTON (p. 842) discuss the epidemiology and control of endemic typhus in Georgia, U.S.A. Control is largely a matter of rat extermination or exclusion. BOSTON (p. 842) indicates the principles of rat control. MUSSER (p. 841) notes that the typhus of Louisiana is entirely of the murine type. PONS (p. 841) reports murine typhus from Porto Rico.

BLANC and BALTAZARD (p. 572) show that there is no loss of virulence in murine virus preserved in the faeces of fleas, so long as the faeces are dry, over a period of 651 days. This long persistence may explain much that is obscure in the carry-over of infection from season to season and country to country.

SPARROW (p. 267) has shown that the virus of murine typhus multiplies abundantly in lice after introduction into the anus. [See also RAYNAL and FOURNIER above.] BLANC *et al.* (p. 262) have shown that the faeces of lice (*Haematopinus asini*), removed from donkeys which had been infected with murine typhus were infective between the 10th and 20th days from the inoculation of the donkeys.

LILLIE *et al.* (p. 572) show that focal typhus nodes are produced in the brains of small rodents such as mice and rats by the virus of endemic typhus, but less constantly by that of Rocky Mountain fever. PANG (p. 261) shows that murine Rickettsiae are able to produce local lesions on the chorio-allantoic membrane of fowl embryo, as well as a generalized infection which often kills the embryo.

FINLAYSON and GROBLER (p. 581) find that guineapigs inoculated with killed Mexican murine virus are protected against the S. African epidemic strain. They also (p. 581) show that the viruses of S. African endemic and epidemic typhus are immunologically identical, but that the murine viruses they have worked with produce only inapparent infection in rats and mice.

Proteus OXK type. Vector: mite.

In the Simla hills WEBSTER (p. 577) has been able to isolate a *Proteus X19* type of virus from rats and a *Proteus XK* type from human cases but not *vice versa*, nor has the *XK* type been isolated from mites on rats, or from the larval *Trombicula deliensis* found on local monkeys.

WOLFF and DE GRAAF (p. 264) report two cases of mite-borne typhus from Java, in which densely populated and highly cultivated island it is, as a rule, rare, though flea-borne typhus is common. A strain of Rickettsia from one of these patients was found to be identical with Sumatran strains and a Malayan strain of scrub typhus. Field rats (*R. rattus brevicaudatus*), from the area in which these men contracted the disease, were examined, but none was found infected; experimental work, however, showed that these rats are able to act as a reservoir for the disease without showing objective symptoms. DELAND (p. 265) notes that cases of typhus seen in New Guinea were of the *Proteus OXK* type with mild symptoms and that no primary sore was seen. DELBOVE (p. 265) notes that both murine typhus and tsutsugamushi are found in Indo-China.

MORISHITA (p. 266) reports a seasonal prevalence of tsutsugamushi in Formosa with its peak in July. The case mortality rate in his series was 12 per cent.

LEWTHWAITE and SAVOOR (p. 576) point out that tsutsugamushi, rural typhus and scrub typhus are identical in all respects. It has been thought that the presence of a primary sore indicated tsutsugamushi and that the absence of this lesion was characteristic of rural and scrub typhus, but the authors do not accept this distinction, since the primary sore may be so slight as to be missed, or may have disappeared at the time of examination. They therefore propose the adoption of the name tsutsugamushi for all these fevers, and that the names rural and scrub typhus should be dropped. The same authors (p. 847) have also examined, by means of pathogenicity and cross immunity tests, strains of the virus of Sumatran mite fever, which they find to be identical with that of tsutsugamushi. KOUWENAAR (p. 846) gives a detailed description of the pathological appearances

found in Sumatran mite fever and in scrub typhus. These appearances are the same in both diseases. They differ from those of classical typhus and endemic typhus in that the chief change is a perivascular infiltration only secondarily attacking the intima, whilst in the classical and endemic forms the primary lesion is destruction of the intima and media followed by perivascular infiltration. KOTTER, however, (p. 577), maintains that there is a valid distinction between Sumatran mite fever and scrub typhus, and refers to the typical primary punched-out ulcer in the former which, he states, is not found in scrub typhus. Sumatran mite fever is very common in the north of the island.

For the second time LEWTHWAITE (p. 847) has isolated a virus identical with stock *Proteus OXK* strains, but which was obtained from a guineapig infected with strain E, originally a *Proteus OX19* strain from rats caught on an estate where tsutsugamushi was present.

LE COSQUINO DE BUSSY and VAN LOGHEM (p. 266) have tested strains of Proteus isolated in Holland against sera from shop and scrub typhus from Sumatra. With shop typhus sera the agglutination was weak, but with scrub typhus sometimes reached a titre of 1 in 10,000, indicating that an X component is inherent in every strain of Proteus. Strongly agglutinated strains completely absorbed Rickettsia agglutinins from the scrub typhus sera.

Indeterminate type. Vector: tick.

GEAR and DE MEILLON (p. 263) state that cases of tick-borne typhus continue to be reported from the Witwatersrand in people associated with tick-infested dogs, and show that *Haemaphysalis leachi*, the dog tick, is capable of transmitting the infection while biting. Guineapigs which have recovered from this infection are not protected against louse-borne or flea-borne typhus, nor do these infections protect against tick-borne typhus. MACVICAR (p. 263) reports four cases of tick-borne typhus at Lovedale, S. Africa.

ROBERTS (p. 260) refers to typhus in Kenya. There is one form which resembles boutonneuse fever, is transmitted from dog to man by *Rhipicephalus sanguineus* and which in one case gave a reaction to *Proteus OXK* but not to *OX19*. In this type there is a primary sore, but there is a second type which resembles murine typhus. LE GAC (p. 575) records a case of apparently tick-borne typhus in Oubangui; the patient's serum showed complete neutralizing power against Rocky Mountain virus, partial against boutonneuse virus, but none against the virus of endemic typhus. SALEUN (p. 263) describes a case of probable boutonneuse fever in Brazzaville.

JOLLY and DI RUGGIERO (p. 266) report a case of typhus from Guadeloupe in which the Weil-Felix reaction to "*Proteus X19* Kingsbury O" was positive at a titre of 1 in 2,500. They state that it resembled boutonneuse fever and was probably transmitted by an Ixodid tick. [The strain of Proteus used is not clear; Guadeloupe is so far from the regions in which the *Proteus OXK* form of typhus (tsutsugamushi) is found that it can hardly have been the same disease.]

Although strains of Rocky Mountain fever virus isolated in the Eastern United States have hitherto been less virulent for guineapigs than those isolated in the West, TOPPING and DYER (p. 843) now report a highly virulent strain recently isolated in Washington, and give details of its effects on guineapigs.

Travassos and Dias (p. 574) have established the identity of the viruses of the spotted fever of Minas Geraes, São Paulo and the Rocky Mountains.

Holland (p. 843) gives information concerning *Dermacentor andersoni* in Alberta, where it is thought to be extending. Ground squirrels and hares are probably the hosts for larvae and nymphs, but domestic stock are the principal hosts for the adults. Open, dry country is less infested than small, deep valleys, since the ticks are sensitive to low humidity. Ticks were found on low bushes and various grasses.

Roberts (p. 844) gives instructions as to the elimination of *Rhipicephalus sanguineus* from dogs and their kennels in Australia. Derris as a powder or wash should be used for the animals, and the kennels should be carefully sprayed with creosote or crude oil, and old bedding should be burned or boiled. [Although this tick has not been associated with human disease in Australia, it is a vector of boutonneuse fever in France and has been suspected in India.]

Topping (p. 575) reports some apparent success in the treatment of experimental Rocky Mountain fever with immune serum, but found (p. 264) prontosil and sulphapyridine to be of no value in this disease.

Vaccination.

In a comprehensive review Murgatroyd (p. 848) has summarized present knowledge of immunization against human rickettsial diseases. Findlay, in discussion of this paper, points out that in N. Africa the natives possess a certain degree of inherited or acquired immunity and that their reactions to vaccination are slight, but that the reactions of Europeans to living vaccines of the murine type are severe. Killed vaccines confer a certain amount of immunity.

In the cultivation of the Rickettsiae of typhus Tchang and Mathews (p. 579) show that inoculation of material into the yolk sac of eggs, avoiding the embryo, gives better results than inoculation into the embryo. Cox and Bell (p. 580) report on the protection afforded to guineapigs by inoculation with the viruses of epidemic and endemic typhus prepared from infected chick embryo. Cox (p. 268) refers to the protective action in animals of a vaccine cultivated in embryonic fowl tissues, and killed with carbolic acid. Zinsser *et al.* (p. 580) obtained profuse growths by infecting minced chick tissue by means of egg yolk cultures, and spreading the tissue over agar surfaces. Zia *et al.* (p. 579) have cultivated the Rickettsiae of epidemic typhus in sterile mouse embryo tissue in human serum Tyrode solution on agar. The growths were killed with Merthiolate and carbolic, and the vaccine thus prepared was found to be non-infective, but capable of producing a positive Weil-Felix reaction.

Macchiavello (p. 255) shows that in infected guineapig tissues, ground, dried and frozen, the European virus remains alive for at least 53 days, the Mexican for 79 days. Either could therefore be despatched for vaccination purposes.

Durand and his fellow workers (pp. 572, 579, 849, 850) have shown that if the viruses of typhus, boutonneuse fever and Rocky Mountain fever are inoculated into mice, rabbits and squirrels by the nasal route, the result is haemorrhagic pneumonia in which masses of Rickettsiae are found in the lungs. These Rickettsiae, emulsified in formalin, have been used to vaccinate guineapigs, and have been successful.

In man and monkeys vaccination by this method produces positive Weil-Felix reactions. CASTANEDA (p. 261) has shown that typhus Rickettsiae produce pneumonic lesions in rats and rabbits.

LAIGRET and DURAND (pp. 266, 267) state that if typhus virus is passaged alternately through the brain and peritoneum of mice there can be produced from the brains a vaccine of high and constant virulence which can be titrated. The mouse brain is emulsified in egg yolk and then dried, it can then be kept for 95 days at refrigerator temperature and has been used successfully for the vaccination of 7,000 persons.

KAWAMURA *et al.* (p. 269) consider that the Pescadores strain of tsutsugamushi, passaged in the testes of rabbits for 181 generations, and producing only mild fever in man, may be used as a vaccine in the endemic regions. This strain has been used in the treatment of general paralysis of the insane.

PINKERTON and BESSEY (p. 268) found masses of Rickettsiae in the peritoneal exudate of rats infected while suffering from riboflavin deficiency, and suggest that this fact might be made use of in the preparation of vaccine.

LAIGRET (p. 850) has experimented with a method of vaccination against typhus by application of a vaccine to the scarified skin.

SPARROW and MARESCHAL (pp. 268, 850) infected men with a murine virus contained in the intestines of inoculated lice, by instillation of an emulsion into the conjunctival sac. Mild fever was produced but no virus could be found in the blood; the men were later found to be immune to inoculation of classical and murine typhus.

BLANC and BALTAZARD (p. 580) show that vaccination with a living murine vaccine attenuated by treatment with bile, in a single dose, produces solid and lasting immunity—in one case for 5 years—against murine and epidemic typhus. The excreta of fleas are dried, and in this state the virus persists for at least two years; treatment with bile, though attenuating the virus, does not alter its infectivity. They (p. 269) state that a febrile attack due to murine typhus, or an inapparent infection produced by bile-treated vaccine will protect against both murine and epidemic typhus for at least 5 years.

MARIANI (p. 578) points out that the non-pathogenic *Rickettsia rocha-limae* is found in a large proportion of lice in Abyssinia. It occurs in louse faeces and may give rise to error in the preparation of vaccine by Weigl's method, and it is possible that the theory of a rickettsial origin of trachoma may have arisen through overlooking this fact.

In a pamphlet sent out by the Pasteur Institute of Algiers (p. 569) it is claimed that immune serum can bestow immediate passive immunity to typhus, and should be used by those investigating outbreaks if they are attacked by lice. The immunity lasts from two to three weeks. Working with concentrated convalescent serum, OVALLE SÁNCHEZ (p. 841) concludes that its injection is harmless but that in prophylaxis its activity is slight if given towards the end of the incubation period.

Q fever.

In investigations on the Rickettsia of Q fever, BURNET *et al.* (p. 253) have found that sera from man and animals infected with other Rickettsial diseases do not agglutinate Rickettsiae of Q fever. The serum of rabbits infected with Q fever virus agglutinates these

Rickettsiae but does not agglutinate any strain of Proteus. Guineapigs protected by Rocky Mountain fever vaccine are not protected against Q fever, but protection against Q fever is active against the virus recovered from wood ticks in Montana, and the serum of patients recovered from Q fever protects against the Montana strain. BURNET and FREEMAN (p. 563) have demonstrated the essential similarity between the Rickettsia of Q fever and the strains isolated from ticks in Montana, except that the latter are the more virulent.

DERRICK and SMITH (p. 851) have found a bandicoot, *Isoodon torosus*, naturally infected with the virus of Q fever in Australia. *Haemaphysalis humerosa* is known to be a natural vector of this disease in animals, and SMITH (p. 851) has investigated its importance in producing infection in man. The faeces of infected ticks are highly infective and are capable of infecting guineapigs even through the unabraded skin. This would appear to be the natural mode of infection of vertebrates, and in some cases abattoir workers may acquire the disease in a similar fashion.

PARKER *et al.* (p. 254) report the finding of Rickettsiae in *Amblyomma maculatum* in Texas, which give complete cross immunity tests with Rocky Mountain and boutonneuse fevers though they are not identical in all respects. COX (p. 254) has shown that this Rickettsia cannot be cultivated in a cell-free medium. The outstanding characteristic is that it can pass through filters, and on this account the name *R. diaporica* is suggested.

DAVIS (p. 562) has recovered *R. diaporica* from *Dermacentor andersoni* captured in Wyoming.

COX and BELL (p. 562) have cultivated *R. diaporica* in tissue culture and in developing fowl embryo. *Charles Wilcocks.*

MALARIA.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

GARDNER (p. 557) calls attention to the increasingly large number of seamen recently arriving in Britain with malaria, which should be borne in mind in diagnosis.

BATES (p. 558) discusses the races of *Anopheles maculipennis*, of which seven may be differentiated in Italy and Albania from egg types. He gives a list of the names given to these races by several workers, with a proposed classification and notes on the geographical distribution.

SYMES (p. 559) discusses malaria in Nairobi, where the only important vector is *A. gambiae*. In the dry season breeding occurs in a few permanent foci only, but with the advent of the rains larvae are to be found in almost every available pool, pit and puddle, most of which are man-made.

RUSSELL and RAO (p. 559) show that in rice fields in Tanjore *A. culicifacies* breeds in wet fields before ploughing, but that breeding is checked when the rice attains a height of 12 inches or more above the water; at this stage *A. hyrcanus* is more plentiful. Intermittent irrigation, with two consecutive dry days each week, prevents the production of adults, and the authors think that the planting of rice

in field channels might control *A. culicifacies* without serious obstruction to the flow of water. Although *A. culicifacies* is the dominant anopheline in the eastern Satpara mountains, WHITE and ADHIKARI (p. 560) believe that it plays only a minor part in malaria transmission. *A. fluviatilis* and *A. varuna* are the principal vectors. WHITE and NARAYANA (p. 561) confirm that in the Singhbhum hills the only vectors are *A. minimus*, *A. fluviatilis* and *A. varuna*, and show that control measures have had considerable success.

GABALDON and his co-workers (pp. 561, 562) show that if mosquito traps are used in stables, more are caught on the first than on subsequent nights. For comparing catches at intervals, therefore, the results on the first night of each period should be chosen. These traps are useful for *A. albimanus*, but not for *A. darlingi* in Venezuela. The mosquitoes can be caught, in traps in which a donkey is the bait, between 7 and 8 a.m., since few anophelines escape before that time.

MER *et al.* (p. 562) show that the red blood cells of malaria patients treated with quinine are laked by bile more quickly than those of untreated malaria patients and much more quickly than those of normal persons.

In patients with quartan malaria who showed oedema, BOYD and PROSKE (p. 563) found conjunction between oedema, albuminuria and reduction in plasma protein, which indicates nephrosis rather than nephritis.

VENHUIS (p. 563) notes that contamination of distilled water, used for Giemsa's stain, with *Bodo caudatus*, a flagellate, may lead to errors in the diagnosis of malaria, since the flagellates may be transferred to the slides and may be mistaken for benign tertian parasites. To prevent this freshly distilled water should be employed.

HILL and CAMBOURNAC (p. 564) conclude that in the Portuguese rice fields the only feasible control measure is intermittent irrigation; water is turned on for 10 days and is then turned off for 7 days. MONDAL (p. 564) describes anopheline control by dry-weather stream training in the Jeypore hills.

RUSSELL *et al.* (p. 564) describe a method of applying Paris green in which the powder is suspended in kerosene and powdered egg albumin, diluted with water and sprayed from a pump. The method is effective, cheap and simple. CHOPRA *et al.* (p. 565) discuss the action of pyrethrum on mosquito larvae.

VANDERPLANK (p. 565) describes certain small fish, closely allied to Gambusia, which are indigenous to East Africa and which should be of greater local value than Gambusia in malaria control.

Bird malaria. BECKMAN (p. 566) estimates the intensity of infection in bird malaria by the time taken to count 20 parasites.

JACOBI (p. 566) records studies on the biology and pathology of *P. gallinaceum*. BELTRAN and LARENAS (p. 567) record observations on the schizogony cycle of *P. gallinaceum*.

TERZIAN (p. 567) reports a study of *P. lophurae* infection in fowls.

RIVERO and RAMIREZ (p. 568) use *Haemoproteus columbae* infections of pigeons for testing the effects of antimalarial drugs. *C. W.*

GARDNER (A.). **Malaria among Merchant Seamen.** [Correspondence.] —*Brit. Med. Jl.* 1941. Jan. 25. p. 134.

The writer of this note calls attention to the increasingly large number of seamen arriving in Britain from malaria infected ports

and to the importance of doctors bearing the possibility of malaria infection in mind when called upon to treat such men. He was recently called to see ten seamen in a ship who were thought to be suffering from gastric influenza. All these men were suffering from malaria. *Norman White.*

COVELL (G.). **Lectures on Malaria.**—*Health Bull. No. 5. Malaria Bureau No. 1.* 33 pp. 1940. Delhi: Manager of Publications. [As. 5 or 6*d*.]

BATES (M.). **The Nomenclature and Taxonomic Status of the Mosquitoes of the *Anopheles maculipennis* Complex.**—*Ann. Ent. Soc. Amer.* Columbus, Ohio. 1940. Vol. 33. No. 2. pp. 343–356. [41 refs.] [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Mar. Vol. 29. Pt. 3. pp. 41–42.]

"Students of the problem agree that the mosquitoes formerly included under the single taxonomic concept of *Anopheles maculipennis*, Mg., form a group of more or less independent populations distinguished by various physiological and morphological characters. There is little agreement, however, regarding the taxonomic categories to which these populations should be assigned, and some twenty latinised names have been applied to them. The author therefore reviews the definitions and general usage of the categories biotype, form, variety, race (geographical and biological), subspecies and species, and recapitulates the points of difference between the *maculipennis* populations, particularly those observed by himself in material from Italy and Albania. He found seven types of eggs, the only difficulties in classification being between *melanoon*, Hackett, and *subalpinus*, Hackett & Lewis, and between *typicus*, Hackett & Missiroli, and *messeae*, Flni. In the first case, the distinction seemed to be purely geographical and thus subspecific, and in the second there appeared to be a phenotypic variation due to temperature. All other characters were found to be definitely correlated with the egg differences. The branching of the antepalmate hair of the fourth and fifth abdominal segments seemed to be characteristic for each population, and it was often possible to identify individual larvae with some certainty. Except for *sacharovi*, Favr (which is shown by hybridisation to be an integral part of the complex), the adults are not readily distinguishable by morphological characters, though there are differences in male genitalia in the case of some of the populations. Physiological differences, correlated with egg types, occur in the ecology of the larvae and their survival in salt solutions and in the epigamic behaviour, food reactions and hibernation of the adults. Hybrids between the populations show various degrees of sterility.

"The author considers that these differences have not been recently evolved and are, in the case of some of the populations, of specific value. He gives an annotated list of the available names in the *maculipennis* group, followed by a proposed classification, with notes on the distribution and synonymy of the species and subspecies he recognises, which may be summarized as follows. *A. maculipennis*, Mg. (*typicus*, Hackett & Missiroli; *basilei*, Flni.) and *A. messeae*, Flni., are widely distributed in Europe, but the latter does not extend so far south as the former. *A. melanoon melanoon*, Hackett, appears to be limited to the Italian peninsula, while *A. melanoon subalpinus*,

Hackett & Lewis, is found in Spain, northern Italy and throughout the Balkans. *A. labranchiae labranchiae*, Flni. (*pergusae*, Missiroli ; ? *sicaulti*, Roub.) seems to be limited to Italy, Spain, certain Mediterranean Islands and north Africa, while *A. labranchiae atroparvus*, van Thiel (*fallax*, Roub. ; *cambournaci*, Roub. & Treill.) is widely but sporadically distributed in central Europe. Their ranges are known to overlap in one district of Italy only. *A. sacharovi*, Favr (with questionable synonyms *elutior*, Martini, *elutus*, Edw., *martinius*, Shing., and *relictus*, Shing.) is a form occurring in the Near East. The name *A. occidentalis*, D. & K., is appended to cover the American representatives of the group, but it is thought that they may include several subspecies, or even species (*aztecus*, Hffm.). The names *alexandrae-schingarevi*, Shing., *lewisi*, Ludl., and *selengensis*, Ludl., are considered to be of uncertain status."

Symes (C. B.). **Malaria in Nairobi.**—*East African Med. Jl.* 1940. Nov. & Dec. ; & 1941. Jan. & Feb. Vol. 17. Nos. 8, 9, 10 & 11. pp. 291–307 ; 332–355 ; 414–430 ; 445–463. With 2 folding charts.

This is a lengthy and somewhat discursive discussion of malaria in Nairobi interspersed with many quotations from many authorities dealing with the public health, social and economic importance of malaria as an endemic disease. The information supplied is mainly entomological and is based upon data collected by the author during routine mosquito surveys from 1926 to 1937. Nairobi has a population of 65,000, which is double that of 1926. The average number of malaria cases a year is about 900, of which 35 are fatal. It is stated that malaria has been a serious problem since the town was established and that its incidence has not decreased during the last ten years. It would appear that no sustained systematic attempts at its control have been undertaken until quite recently. Eighteen species of Anopheles have been found in Nairobi. The only vector of importance is *A. gambiae*. During the drier months larvae are to be found in relatively few permanent breeding places. Soon after the early rains of February or March breeding becomes much more extensive until June when larvae are to be found in great numbers in almost every available pool, pit and puddle. The majority of these breeding places are man-made. Suggestions are made for permanent control ; stress is laid on the desirability of abolishing the ideal facilities for *A. gambiae* breeding that are provided by the irrigation channels of the " swamp " used for market gardening. *N. W.*

Russell (Paul F.) & Rao (H. Ramanatha). **The Anopheles of Ricefields in South-Eastern Madras.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 427–446. With 1 chart & 10 figs. on 5 plates.

This is a further contribution to the study of malaria in the Pattukkottai Taluk of the Tanjore District [see this *Bulletin*, 1939, Vol. 36, p. 131]. Studies have been made to determine the importance of ricefields in the propagation of malaria and to obtain information regarding the breeding of all species of Anopheles in relation to season, stage of growth of rice, and the state of the ricefield. Rice culture is described. Ten species of Anopheles larvae were found in ricefields, *A. annularis*, *barbirostris*, *culicifacies*, *hyrcanus* var. *nigerrimus*, *jamesi*,

pallidus, *subpictus*, *tesselatus*, *vagus* and *varuna*. The commonest species in fallow fields were *A. subpictus*, *culicifacies* and *pallidus*; *A. culicifacies*, the vector, was most prevalent in wet fields prior to ploughing; it was not abundant in nurseries. When the rice had attained a height of 12 inches above the water surface the breeding of *A. culicifacies* was checked. Thereafter *A. hyrcanus* became more plentiful. It seemed probable that the distribution and density of species was more dependent upon the stage of the rice than on the season of the year. The production of adult mosquitoes could be prevented by intermittent irrigation, 2 dry days and 5 wet, except during periods of daily rain. The planting of rice in field channels might control the breeding of *A. culicifacies*, after the rice was 12 inches or more above the water surface, and this without serious obstruction to the flow of water. *N. W.*

White (R. Senior) & Adhikari (A. K.). **On Malaria Transmission in the Eastern Satpura Ranges.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 383–411. With 1 map & 1 chart.

From September 1936 to April 1940 continuous observations have been carried out in the neighbourhood of thirteen stations on either side of the Maikal Range which forms the eastern limit of the Satpura ranges, in the Central Provinces. The area is mainly forest, with clearings in which rice is grown during the rains. All but the larger streams dry up during the hot weather. The indigenous population are aboriginals, Ghonds and Bhaigas. In some areas malaria endemicity is low but here malaria epidemics at the close of the rains occur. In other areas endemicity is very high. No work on malaria transmission in the Central Provinces had been done during the twenty years prior to this inquiry. Kenrick (1914) believed that *A. culicifacies* was the important vector in the Central Provinces [this *Bulletin*, 1915, Vol. 5, p. 38].

Nineteen species of anophelines were encountered during the observations now reported: *A. culicifacies*, *A. fluviatilis*, *A. varuna*, *A. minimus*, *A. aconitus*, *A. jeyporiensis*, *A. splendidus*, *A. maculatus*, *A. theobaldi*, *A. karwari*, *A. stephensi*, *A. tesselatus*, *A. jamesi*, *A. annularis*, *A. pallidus*, *A. barbirostris*, *A. hyrcanus* var. *nigerrimus*, *A. subpictus* and *A. vagus*. Dissections of specimens of all these were made with the exception of the last four. *A. culicifacies* is the dominant species; infective specimens were found in only two of the thirteen localities studied and the sporozoite rate was very low. The authors believe it to play a very minor part in malaria transmission. *A. fluviatilis* had a high sporozoite rate in ten of the thirteen localities; sporozoites were found every month from September to December. *A. varuna* was only one-third as plentiful as *A. fluviatilis* in house catches but it had an even higher sporozoite rate; infective specimens were found as early as August. These two species, *A. fluviatilis* and *A. varuna*, are the two chief vectors in hyperendemic tracts. They show wide variations from place to place, and from year to year, in the numbers resting in houses. *A. minimus* is very rare. Both *A. annularis* and *A. pallidus* were found infected but neither is thought to be of any importance in malaria transmission. In a severe epidemic in one of the stations, Dongargarh, research failed to incriminate any species as the chief vector. *N. W.*

White (R. Senior) & Narayana (P. Appal). **On Malaria Transmission in the Singhbhum Hills. Part II. An Experiment with Trap-Nets.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 413–425.

In a previous paper Senior White and Das reported that the only malaria vectors in the Singhbhum Hills were Anopheles of the *funestus* group [this *Bulletin*, 1939, Vol. 36, p. 14]. It was also shown that transmission occurs throughout the year except in the three months May to July. To confirm these conclusions a human-bait trap-net was set up in the village of Kolhadi, where malaria is hyperendemic, and a similar trap-net about a mile away in the centre of a protected area in Dangoaposi station. The results of twelve months' catches in these trap-nets are recorded. Since 1938, anti-larval measures at Dangoaposi have been restricted to the *funestus* group. The catches at Kolhadi show that there are no anophelines biting between March and June; that the *funestus* group is not present in any quantity till the end of August; oöcysts were found in *A. minimus* in the last week of August and sporozoites in *A. varuna* in the first week of September. The last sporozoites were found in *A. fluviatilis* in mid-November. The nights are cold in December and transmission appears to stop. Comparing the catches of the two stations it would appear that control of *A. varuna* in Dangoaposi is complete; that *A. minimus* has been reduced by more than 90 per cent.; and that nearly a third of *A. fluviatilis* remain uncontrolled. The vectors only penetrate the controlled area in any numbers in September and in the first half of October. It is confirmed that in the Singhbhum Hills the only malaria vectors are *A. fluviatilis*, *A. minimus* and *A. varuna*.

N. W.

Roy (D. N.). **A Study of the Bionomics of** *Anopheles subpictus* **and** *Anopheles annularis*.—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 499–507. With 6 figs.

Venkat Rao (V.) & Ramakrishna (V.). **A Note on the Larva of** *A. varuna* **(Iyengar).**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 509–512.

Overbeek (J. G.). Malaria-onderzoek in de Kolonisatie Belitang (Residentie Palembang) in April 1940. [**Malaria Investigations in Belitang.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. Sept. 10. Vol. 80. No. 37. pp. 2166–2177. With 1 plan.

Gabaldon (Arnoldo), Antonio Lopez (Jose) & Ochoa-Palacios (Manuel). Estudios sobre anofelinos. Serie I. 4. Variaciones curiosas de cuentas diarias de anofelinos en trampas-establo. [**Daily Variations of Anophelines Caught in Animal Traps.**]—*Publicaciones de la Division de Malariologia.* Ministerio de Sanidad y Asistencia Social. Caracas. 1940. Aug. 15. No. 5. pp. 33–39. English summary.

"From the experiments reported in this paper the following facts were noted:

"1. A baited stable-trap in one location caught more anophelines the first night than it did the second and third nights.

"2. When a trap was observed for nine consecutive nights, the catches during the last six were smaller than those on the first night and compared with those of the second and third.

"3. These findings call attention to what appears to be a curious anopheline psychology for we do not have any explanation. If they are confirmed, it may be concluded that daily consecutive readings of a baited stable-trap in the same position give figures that are about one-third the actual number of anophelines caught if the trap is used only one night in a new position. It follows, therefore, that weekly or monthly catches will be comparable only if the trap is used one night in a particular location of each determination."

GABALDON (Arnoldo), OCHOA-PALACIOS (Manuel) & PEREZ-VIVAS (M. A.). Estudios sobre anofelinos. Serie I. 5. Observaciones sobre lecturas de trampas-establo con cebo animal. [**Results Obtained with Animal Traps for Anophelines.**]—*Publicaciones de la Division de Malariologia.* Ministerio de Sanidad y Asistencia Social. Caracas. 1940. Aug. 15. No. 5. pp. 41–56. English summary.

"The catches of adult anophelines in stable-traps give information on the density of zoophilic [species] and the efficiency of the anti-larval measures. In Venezuela this kind of trap is useful where *A. albimanus* is the main vector, but *A. darlingi*, the other important one, is not caught by these traps. As the anophelines were active before sunrise the present experiments were carried out in order to see if they escaped before the catch was made at 7 to 8 a.m. A donkey was used as bait. Less than three per cent. of the mosquitoes caught escaped before sunrise. It is believed that such amount is insignificant to be taken into consideration as source of error when the catches are made after sunrise. No species showed a particular trend to escape more than another, but in general, the 'Nyssorhynchi' escaped more than the 'Arribalzagias,' although the difference probably is not significant."

MER (G.), BIRNBAUM (D.) & KLIGLER (I. J.). **Lysis of Blood of Malaria Patients by Bile or Bile Salts.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 373–378.

Experiments were made to determine the relative sensitivity of normal and malarial blood, respectively, to lysis. Tubes of 6 mm. diameter were used. Into each tube was placed 0·3 cc. of a 0·3 per cent. saline solution of dried ox-bile (Difco) and one drop of fresh blood. The blood was uniformly suspended by shaking and the tubes were placed in an incubator at 37°C. until haemolysis was complete. The time required for complete haemolysis was the index of the sensitivity of the cells. Red cells of normal individuals laked in from 4½ to 5 hours. Red cells of malaria patients laked in about 3 hours, the range being from 2½ to 5 hours depending on the duration of the attack. The red cells of malaria patients treated with quinine laked in from half an hour to 3 hours. Quinine or quinine-plasmoquine treatment increased the sensitivity to laking of the blood of malaria patients. The observations form an interesting contribution to the study of the aetiology of malarial haemoglobinuria. *N. W.*

Boyd (Mark F.) & Proske (H. O.). **Observations on the Blood Proteins during Malaria Infections.**—*Amer. Jl. Trop. Med.* 1941. Mar. Vol. 21. No. 2. pp. 245–260. With 6 charts.

This is a record of observations on the proteins of the blood plasma of patients undergoing malaria therapy. It was hoped that such observations might throw light on the nature of the oedema sometimes observed in such patients. In a group of eight patients blood was collected for analysis during the incubation period and thereafter, usually twice a week, till the expiration of the clinical attack or later. Only one of these patients developed oedema; he had a quartan infection. The second group consisted of two patients who developed oedema some time after the onset of a malaria attack when observations on plasma proteins were begun. A routine examination of urine for albumin and casts was carried out weekly. Ten cc. of blood were placed in a sterile centrifuge tube containing 10 mgm. of dry purified neutral potassium oxalate. An estimation was made of the total protein, albumin, total globulin, and fibrin in the blood plasma. An estimation of euglobulin was made in a separate portion of serum.

No oedema occurred in five patients infected with *P. vivax*. It occurred in one of three patients infected with *P. falciparum* and in both of the two patients infected with *P. malariae*. In the *P. vivax* patients plasma albumin was reduced but the reduction was not always accompanied by the appearance of albumin in the urine. In the *P. falciparum* patients albuminuria was more constantly associated with a depression in the plasma albumin but oedema was not significantly associated with such depression. In the patients infected with *P. malariae*, albuminuria, a depression in plasma albumin and oedema appeared to be definitely associated. The conjunction of oedema, albuminuria and the reduction in plasma protein indicates that malaria infection produces a nephrosis rather than a nephritis. *N. W.*

Venhuis (W. G.). Bodo caudatus in bloedpraeparaten. [*Bodo caudatus* **in Blood Films.**]—*Geneesk Tijdschr. v. Nederl.-Indië.* 1940. July 30. Vol. 80. No. 31. pp. 1835–1841. With 3 figs. on 1 plate. English summary.

"From a sanitated, formerly malarious area, which is under constant supervision, an outbreak of malaria was reported. Larval and adult catches did not reveal anything wrong. So the attention was directed to the diagnosis of malaria. From the local Doctor we got over 30 thick films to check up. All these blood samples did not contain a single malarial parasite, but all of them showed a flagellate namely Bodo caudatus, mostly in rather small numbers. These flagellates were mistaken for large trophozoites, younger schizonts or gametocytes of benign tertian malaria. The cause of all the trouble, the Bodo, could be found in the distilled water, used for dilution of Giemsa's stain.

"Only in one of the blood samples some of the flagellates showed their flagellae, in all the others they could not be seen at all. Only after restaining, the flagellae could be made quite clear.

"During the year 1939 two cases of this contamination were observed.

"The use of fresh distilled water will prevent this error."

HILL (Rolla B.) & CAMBOURNAC (Francisco J. C.). **Intermittent Irrigation in Rice Cultivation, and its Effect on Yield, Water Consumption and Anopheles Production.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 123–144.

Malaria in Portugal is almost limited to rice-growing districts of the south; here the disease is hyperendemic. Experiments with intermittent irrigation of ricefields have been carried on since 1935. It has been consistently found that the periodic drying of the ricefields greatly reduces the number of mosquito larvae, decreases the amount of water necessary for cultivation, and, with most varieties of rice tested, increases the yield without detriment to quality of the grain. The water was turned on for 10 days; then the field was drained, the water being turned off for, usually, 7 days. The complete Anopheles cycle, in local conditions, occupies at least 18 days. Under ordinary field conditions a reduction of over 80 per cent. in the number of anopheline larvae found can be secured by intermittent irrigation. Special preparation of the fields is required. The conclusion is reached that intermittent irrigation is the only feasible method so far evolved for the control of Anopheles breeding in the ricefields of Portugal.

N. W.

MONDAL (R. S.). **The Species Control of a Hill-Stream by Training.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 465–474. With 3 figs. on 1 plate.

The author describes a stream in the Jeypore Hills which in the dry season meandered in a bed, in part sandy and in part boulder-strewn, between high earth banks which form the flood season margins. Along the grass edges and among tree-roots *A. fluviatilis* and *A. varuna*, the local vectors, bred in profusion. Larvae of these species are very rarely found near sand or boulder edges. When the river subsides in January training of the stream becomes possible; this is accomplished by a gang of six men with a sand plough and some spade work. This training renders oiling unnecessary from January till the rains break early in June, some 20 weeks, along the 1½ miles of stream in which mosquito breeding is controlled. *N. W.*

RUSSELL (Paul F.), KNIPE (Fred W.) & RAO (T. Ramachandra). **On using Water instead of Dust for diluting Paris Green in Malaria Control.**—*Indian Med. Gaz.* 1940. Dec. Vol. 75. No. 12. pp. 740–742. With 1 fig.

This dustless method of diluting and spreading Paris green was first described by BARBER, RICE and MANDEKOS [this *Bulletin*, 1937, Vol. 34, p. 170]. The authors of the present paper have modified the original method and have used it with marked success. A stock suspension contains kerosene oil 400 cc., Paris green 200 cc. and dry powdered commercial egg albumin 1 gm. The ingredients are put, in the order mentioned, into a Winchester bottle, which is then well shaken. The mixture is carried to the scene of operations in corked glass vials, 4 inches by 1 inch; each vial contains 25 cc. of the stock suspension. A khaki drill belt, of the cartridge belt type, enables a coolie to carry from 20 to 25 filled vials. The remaining equipment consists of a tin measuring exactly 1,000 cc., a tin funnel with a wire

gauze sieve, and a Hudson Sterling No. 115 sprayer. On arrival at the breeding place 2 litres of water are strained into the sprayer tank to which the contents of one vial, after vigorous shaking, are then added. Shaking with a little more water removes the last traces of Paris green from the vial. Three more litres of water are then added to the sprayer tank. The pump plunger is replaced and pumped to the desired pressure. The sprayer is slung on the back and spraying is done with the nozzle 1 to 1½ feet above the water surface. One vial of stock suspension is enough to cover about 500 square feet of water surface. Mosquito breeding was effectively controlled even in the presence of considerable vegetation. The method is effective, cheap and simple. *N. W.*

Chopra (R. N.), Roy (D. N.) & Ghosh (S. M.). **Action of Pyrethrum on Mosquito Larvae.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 457–463. [16 refs.]

The authors describe laboratory and a few field experiments on the mosquito larvicidal properties of Pyrethrum preparations. Quite small quantities of Pyrethrum powder can destroy all types of mosquito larvae in the laboratory ; in the field, however, its larvicidal properties are feeble. Small fish such as *Panchax panchax* are affected much more quickly than are anopheline larvae. The action of kerosene oil on mosquito larvae is enhanced by the addition of Pyrethrum ; the spreading power of the oil is greatly increased thereby. An aqueous extract of Pyrethrum has insecticidal properties, although the two active principles, pyrethrin I and II, are insoluble in water. The solid residue after the removal of pyrethrin I and II has both insecticidal and larvicidal properties. The insecticidal properties of Pyrethrum cannot always be correlated with its pyrethrin content. *N. W.*

Vanderplank (F. L.). **Nothobranchius and Barbus Species : Indigenous Anti-Malarial Fish in East Africa.**—*East African Med. Jl.* 1941. Jan. Vol. 17. No. 10. pp. 431–436. With 3 figs.

There are several species of small fish indigenous to East Africa and closely allied to Gambusia which, from the anti-malaria point of view, should be of greater local value than Gambusia. Some of these are described.

The genus Nothobranchius belongs to the Family Cyprinodontidae (egg-laying tooth carps). Gambusia belongs to the Family Poeciliidae (live-bearing tooth carps). Four species of Nothobranchius have been recorded from East Africa ; it is probable that they are identical with or at most varieties of *N. taeniopygus*. The male fish attains a length of 1¾ in., the female 1½ in. It occurs in seasonal pools but has not been taken from seasonal streams or rivers. The young develop from desiccated eggs in the dried mud at the beginning of the rains. They take 6 to 8 weeks to become full-grown. They are voracious feeders. Once adult the female lays from 20 to 100 eggs a day for the rest of her life, which may be till the pool dries up. The eggs take 60 to 70 days to hatch unless they become desiccated ; desiccated eggs begin developing immediately they are reimmersed in water. Adults prey upon their young as do adult Gambusia. Nothobranchius stand a range of temperature from 50° to 105°F.

Three species of Barbus have been investigated, *B. taitensis*, *B. innocens*, and a new species discovered by the author. The maximum length of the first named is 2½ in.; of the other two 2 in. They are indigenous to rivers and stagnant pools in East Africa. They eat greedily all mosquito larvae offered to them but they are not primarily "live-feeders" as are Nothobranchius. Nothing is known of their breeding habits. They reappear in streams and rivers that completely dry up during the dry season.

Pachypanchax playfairii is found along the East African coast in stagnant waters and small streams. It prefers mosquito larvae to other foods. Its maximum length is 3½ in. *N. W.*

Beckman (Harry). **An Experimentally Derived Method for Determining the Degree of Infection in Avian Malaria.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 151–157. With 5 figs.

The study of the blood of canaries infected with *Plasmodium cathemerium* has led the author to adopt a method of recording the intensity of infections based on the time occupied in counting twenty parasites in thin blood films. A time limit of three minutes is arbitrarily chosen. A negative record indicates that no parasites were seen in a three minutes' search, while a 1+ means that less than twenty were seen in the same time. A 2+ is recorded when the twenty parasites are seen in 2–3 minutes, 3+ when seen in 1–2 minutes, 4+ in half to one minute and 5+ in half a minute or less. The author has used the method in his experimental work and finds it reliable for determining the degree of infection upon a comparative basis.

C. M. Wenyon.

Jacobi (Ludolf). Zur Biologie und Pathologie des Plasmodium Gallinaceum (Brumpt). [**Biology and Pathology of** *P. gallinaceum.*]—*Arch. f. Experim. Path. u. Pharm.* 1940. Dec. 12. Vol. 196. No. 6. pp. 623–643. With 2 figs. [27 refs.]

In a study of *Plasmodium gallinaceum* the author has shown that parasites appear in the blood a few minutes after intramuscular inoculation of a fowl with infected blood from another fowl. Similarly, parasites appear in the blood immediately after intravenous injection of a much smaller dose, and most of the parasites thus injected continue their development. Nevertheless, the older the parasites injected, particularly when approaching schizogony, the greater is the number which continues the development. Two-hourly blood examinations showed that there is no clear-cut cycle of development. At most only 70 per cent. of the parasites were in any one stage of development at any moment. Chronically infected birds reveal a marked immunity to superinfection. Of 32 birds inoculated intravenously, only 5 showed any development of the parasites introduced, and in not one of these did the development lead to an acute infection, as is always the case with birds not previously infected. Birds which have clinically recovered still harbour parasites for at least 1½ years, as shown by the fact that 0·05 cc. of blood will infect new birds. As regards exoerythrocytic schizonts, these could not be found in superinfected birds between the 10th and 74th days, even after intravenous injections of heavy doses of parasites. Heavily infected blood in citrate solution

retains its infectivity for four days at laboratory temperature but there is, during this period, a continual death of the parasites. The plasma from this citrated blood loses its infectivity in 24 hours, but if blood from a healthy fowl is added to it its infectivity is not lost in this period. In this case it cannot be supposed that the survival is due to the protection afforded by a host cell. *C. M. W.*

Beltran (Enrique) & Larenas (Raúl). El ciclo esquizogónico en *Plasmodium gallinaceum* Brumpt. [**Schizogony Cycle in** *P. gallinaceum*.]—*Rev. Inst. de Salubridad y Enfermedad. Trop.* Mexico. 1940. Dec. Vol. 1. No. 4. pp. 291–309. With 4 graphs. [14 refs.] English summary (8 lines).

A study of the schizogony cycle in *Plasmodium gallinaceum* has shown that this occupies from 36 to 42 hours. There is a high degree of synchronicity, the majority of the parasites reaching maturity at one time. There is, however, considerable variation in this respect from bird to bird. Though there was a notable mortality of all stages of the parasite from the merozoite to the mature schizont, this was not so marked as that reported for certain other malarial parasites of birds. *C. M. W.*

Terzián (L. A.). **Studies on** *Plasmodium lophurae*, **a Malarial Parasite in Fowls. I. Biological Characteristics.**—*Amer. Jl. Hyg.* 1941. Jan. Vol. 33. No. 1. Sect. C. pp. 1–22. With 2 figs. [10 refs.]

The author has carried out a biological study of *Plasmodium lophurae*, the malarial parasite of a Borneo fireback pheasant, which was inoculated by Coggeshall to young chicks. To maintain the parasite satisfactorily in chicks, intravenous inoculations of at least 50,000 parasites must be made, and transfers are best made every five or six days. Parasites remain in the blood for five to fourteen days. Three or four days after parasites disappear from the blood this is no longer infective to fresh chicks, though it has been shown that parasites are still present. The numbers are too low to bring about visible infections in new chicks inoculated with the blood. The length of the asexual cycle has been shown to be 48 hours, but the actual schizogony cycle occurs continuously over a period of 12 hours, the synchronicity being low. The gametocytes appeared in the blood at the same time as the asexual forms and increased in number from day to day in the same relative proportion to the asexual forms. The gametocytes occupied 48 hours to grow to maturity and they were destroyed a few hours after this. There was little destruction of merozoites, the majority of which successfully invaded red blood corpuscles. The destruction of the asexual stages occurred at a later stage of growth, when no doubt the infected red cell had been sufficiently altered to render it susceptible to phagocytosis. A study of the internal organs showed that the parasites were not present in any greater concentration than they were in the peripheral blood. No evidence of exoerythrocytic schizogony was obtained.

C. M. W.

Rivero (María de los Dolores) & Ramirez (Eliseo). La infección por el *Haemoproteus columbae* en la investigación de la actividad antimalárica. [**Infection by *H. columbae* for testing Antimalarial Efficiency.**]—*Rev. Inst. Salubridad y Enfermedad. Trop.* Mexico. 1940. Sept. Vol. 1. No. 3. pp. 245–264. With 14 figs. [14 refs.]

The authors describe the life cycle of *Haemoproteus columbae* of the pigeon and advocate the use of this parasite as a means of testing antimalarial drugs. They show that the gametocidal action of plasmoquine and the schizonticidal action of quinine are exemplified by the influence they have on the life cycle of the parasite of the pigeon, just as they have been shown to have on *Plasmodium cathemerium* infections in the canary. It has been possible to demonstrate that extracts of the husk of *Coutarea latiflora*, which is popularly regarded as a remedy for malaria, has no effect on the life cycle of *H. columbae* when administered to infected pigeons.

C. M. W.

LEISHMANIASIS.

Précis of Abstracts in this Section.

Visceral. Clow (p. 569) reports that kala azar is widespread in the Shensi province of China. He discusses diagnosis and treatment; cancrum oris has been noted as a complication in a number of cases.

Chung and Li (p. 570) produce further evidence which favours the view that human kala azar in the region of Peiping is closely bound up with the disease in dogs. Galliard (p. 570) discusses the view expressed by Chung, that dogs are reservoirs of kala azar in Peiping, and points out that, though in the legations quarter of the city canine kala azar is common, cases of human disease there are rare.

Ajello (p. 570), from a study of canine leishmaniasis, concludes that the cutaneous lesions are part of a general invasion of the reticulo-endothelial system, which affects also the internal organs. Ho *et al.* (p. 571) describe the diagnosis of canine kala azar by means of ilium puncture. Mello (p. 571) reports a natural infection of a cat with a species of leishmania in Brazil.

Pai and Hu (p. 571) report failure to cultivate *Leishmania donovani* in tissue culture.

Chu and Zia (p. 572) show that after intratesticular inoculation of hamsters with *L. donovani* the parasites can be readily demonstrated five days later by testicular puncture.

Paraense and Chagas (p. 572) have shown that *Phlebotomus longipalpis* and *P. intermedius* may become naturally infected with the parasites of S. American visceral leishmaniasis.

Davies and Wingfield (p. 572) confirm the work of Kirk and Sati on the value of gland puncture in diagnosis. They report a case of agranulocytosis occurring in a patient who had received 2·6 gm. of neostibosan; injection of adrenalin produced improvement and the patient recovered. Andreu Urra *et al.* (p. 573) advocate sternal puncture in diagnosis.

Cook (p. 573) reports a case in an Indian seaman admitted to hospital in New Zealand.

Kirk and Sati (p. 573) report further experiences with certain aromatic diamidines in the treatment of kala azar in the Sudan. The results were eminently satisfactory, even in the presence of complications such as cancrum oris and even when treatment with antimonials had failed. Details of dosage are given. Napier and Sen (p. 574) report that diamidino-stilbene appears to be an effective therapeutic agent in the treatment of kala azar, and give details of the dosage they employ. Unpleasant effects are sometimes produced but may be relieved by the injection of adrenalin.

Wang and Chung (p. 575) produce evidence which suggests that hamsters cured of infection with *L. donovani* by treatment with neostibosan are immune to reinfection.

Cutaneous and muco-cutaneous. Sallam (p. 575) describes the clinical features of oriental sore in Egypt; tartar emetic, either injected or as an ointment, is very useful in treatment.

Senekji and Beattie (p. 576) have infected 200 persons with suspensions of *L. tropica* in Bagdad. In each case a sore was produced and though reinfection was possible if attempted before the healing of the primary sore, it could not be effected once healing was complete. Templeton (p. 576) reports a case of oriental sore experimentally produced.

Orsini (p. 576) points out that leishmaniasis is becoming an urgent problem in Minas Geraes, and that in the majority of cases mixed mucosal and cutaneous lesions are found.

For the skin lesions of American leishmaniasis Mazza and Cornejo (p. 577) have found local infiltration with atebrin solution, and atebrin by the mouth, to be a very satisfactory treatment. *C. W.*

Clow (J. Menzies). **Shensi Province as an Endemic Focus of Kala-Azar. A Preliminary Report.**—*Chinese Med. Jl.* 1941. Feb. Vol. 59. No. 2. pp. 150–155.

Kala azar appears to be widespread in the Shensi province of China, judging from the records of the Jenkins Robertson Memorial Hospital at Sian. In March 1940 a special clinic for cases of this disease was started at the hospital and by November 196 cases (93 per cent. diagnosed by the finding of leishmania) had been dealt with. Of the first hundred cases 68 were from the province of Shensi itself and all of these except about twenty were in children who had never left the area. The thirty odd cases from outside provinces were mostly in adults. A list of the villages from which the cases came is given. For diagnosis sternal puncture is advocated in preference to spleen or liver puncture. Treatment was carried out by intravenous injections of neostam or ureastibamine thrice weekly. It is stated that vomiting is common with neostam, while anaphylactic shock was seen four times with ureastibamine. Of complications cancrum oris was noted in 14 cases either before or during treatment. The mortality from this complication was about 64 per cent. The records of the treated cases are not entirely satisfactory. It is evident that the province of Shensi, in which the incidence of the disease must be very high, affords an excellent opportunity for an investigation of the epidemiology of kala azar. *C. M. Wenyon.*

CHUNG (Hui-Lan) & LI (T. C.). **The Occurrence of Canine Leishmaniasis in Kala-Azar Villages in the Suburbs of Peiping.**—*Chinese Med. Jl.* 1940. Dec. Vol. 58. No. 6. pp. 661–670. With 1 map.

In an earlier paper [this *Bulletin*, 1941, Vol. 38, p. 252] attention was called to the close relationship between human and canine kala azar in Peiping. There was strong presumptive evidence that the dog was actually a reservoir of the virus. In the present paper the authors produce further evidence derived from a study of the relationship in three villages near Peiping—namely Huaifang, Ch'engfu and Haitien. All these places have been known to be endemic centres of the human disease and in the first of them all the cases in the village were discovered and treated in 1937 in the hope that this would stamp out the disease. Cases, however, continued to occur. When the study of the distribution of canine kala azar in Peiping had yielded such significant results this was extended to the three villages mentioned. Here again the disease was found to be common in dogs. At Huaifang 5 out of 65, at Ch'engfu 6 out of 16, and at Haitien 6 out of 12 dogs were found infected. At the two first mentioned places there was a very close association of the canine and human kala azar. At Haitien, a much larger place, it was not possible to draw any definite conclusions. It is suggested that the persistence of the human disease in Huaifang after 1937 was due to the continued presence there of the canine disease. *C. M. W.*

GALLIARD (H.). A propos du kala-azar humain à Peiping. [**Human Kala Azar in Peiping.**]—*Chinese Med. Jl.* 1941. Feb. Vol. 59. No. 2. pp. 156–157.

The author refers to a paper by CHUNG [this *Bulletin*, 1941, Vol. 38, p. 252] on the relationship between human and canine kala azar in Peiping. Chung's conclusion was that the relationship is so close that there is reason to believe that, as in the Mediterranean areas of infection, the dogs of Peiping are reservoirs of the virus. The author of the present paper, while not disputing the general conclusion, points out that though in the legations quarter of the city canine kala azar is common, cases of the human disease there are rare. There appear to be records of only three. The first was that of a German soldier who died after return to Germany in 1900, the second was of a French soldier diagnosed in Strasbourg in 1925 and the third of the child of a Japanese diplomat. The author recalls that he and BRUMPT [this *Bulletin*, 1935, Vol. 32, p. 486] described experiments with the virus obtained from the case of the Frenchman, in which they demonstrated the susceptibility to inoculation of the European spermophile (*Citillus citillus*) and the Palestinian hamster (*Cricetulus auratus*). *C. M. W.*

AJELLO (P.). Contributo allo studio delle ulcere cutanee nella leishmaniosi del cane. [**Study of Skin Lesions in Canine Leishmaniasis.**]—*Nuova Ercol.* 1939. Vol. 44. pp. 281–300. [Summary taken from *Vet. Bull.* 1941. July. Vol. 11. No. 7. p. 436. Initialled U. F. R.]

Histological investigations were carried out on 14 cases of cutaneous leishmaniasis of dogs to ascertain the nature of the lesion and the

relationship between cutaneous and visceral leishmaniasis. It is pointed out that leishmanial ulcers are indistinguishable macroscopically from traumatic or trophic ulcers, that they are often the only symptom of leishmaniasis observed, and that they usually occur on skin areas exposed to trauma. In dogs the ulcer is not preceded by a nodule as in human beings.

In all the cases under investigation visceral leishmaniasis was found to be present. The essential lesion appears to be an invasion of the lower layers of the skin with histiocytes, combined with degeneration and necrosis of the epidermal cells. It is concluded that cutaneous canine leishmaniasis is not a separate entity, but that the parasites with their predilection for reticulo-histiocytic tissue invade the skin and internal organs with equal readiness.

Ho (E. A.), Chu (H. J.) & Yuan (I. C.). **Ilium Puncture, a Simple Method for obtaining Bone Marrow from Dog.**—*Chinese Med. Jl.* 1940. Dec. Vol. 58. No. 6. pp. 679–681. With 2 plates.

For the diagnosis of kala azar in dogs the authors, who have had experience in North China, advocate ilium puncture. This is carried out by use of a short intravenous injection needle fitted with a stylet. The dog is placed on its side and the needle is passed in an antero-posterior direction through the skin and muscles till it impinges on the ilium just behind the crest. It is then bored through the outer lamina of the bone till a yield in resistance indicates entry into the spongy bone of the marrow cavity. The stylet is then withdrawn and, with an ordinary 20 cc. syringe fitted to the needle, bone marrow is sucked up. It has been found that the method is applicable to cats and rabbits. *C. M. W.*

Mello (G. Britto). Verificação da infecção natural do gato (*Felix domesticus*) por um protozoario do genero Leishmania. [**Natural Infection of a Cat with** *Leishmania* **sp.**]—*Brasil-Medico.* 1940. Mar. 23. Vol. 54. No. 12. p. 180.

In the district of Aurá, about thirty kilometres from Pará, a cat was discovered suffering from ulceration of the ears and nose. Examination of smears revealed what appeared to be leishmania. It was realized that these might be leishmania stages of *Trypanosoma cruzi*, so a number of detailed examinations were carried out. Blood smears failed to reveal trypanosomes, while leptomonads developed in culture media inoculated from the sores. Sections of tissue showed distribution of leishmania in mononuclear cells. Bugs (*Triatoma brasiliensis*) fed on the sores acquired only a transitory leptomonas infection. This and other tests indicated that the parasite was of the genus *Leishmania*, but whether *L. brasiliensis* or *L. chagasi* could not be determined. *C. M. W.*

Pai (H. C.) & Hu (C. H.). **Attempts to grow** *Leishmania donovani* **in Tissue Cultures.**—*Proc. Soc. Experim. Biol. & Med.* 1941. Apr. Vol. 46. No. 4. pp. 606–608. With 2 figs.

"Attempts to grow *Leishmania donovani* were made in cultures of chicken, hamster and human tissues. It was found that the parasites were taken up by the phagocytes within 24 hours. In the hanging drop cultures parasites were all degenerated by the 15th day. In the

slowly growing cultures in flasks prepared according to Fischer and Parker's method they were all degenerated by the 43rd day. Multiplication of the parasites has not been observed.

"It is concluded that the parasites may survive for various lengths of time but cannot grow in the tissue cultures according to the methods described, and that the length of survival is in inverse ratio with the rapidity of the growth of the tissue cultures."

CHU (H. J.) & ZIA (Samuel H.). **Leishmania Infection of Hamsters and Rabbits by the Intratesticular Route.**—*Chinese Med. Jl.* 1940. Dec. Vol. 58. No. 6. pp. 677–678.

The authors have found that Chinese hamsters can easily be infected with *Leishmania donovani* by intratesticular inoculation. The presence of parasites can readily be detected by testicular puncture sometimes as early as the fifth day. Systemic involvement can be demonstrated within two weeks of inoculation. It was shown that a local infection lasting for one month followed intratesticular inoculation of the otherwise resistant rabbit. *C. M. W.*

PARAENSE (L.) & CHAGAS (A. W.). Transmissão experimental da leishmaniose visceral americana pelo *Phlebotomus intermedius*. Nota prévia. [**Experimental Transmission of American Visceral Leishmaniasis by** *P. intermedius*.]—*Brasil-Medico.* 1940. Mar. 23. Vol. 54. No. 12. pp. 179–180. With 2 figs.

It has already been shown in South America that sandflies (*Phlebotomus longipalpis* and *P. intermedius*) become infected with leptomonads when fed on dogs suffering from kala azar. To obtain proof that these flagellates in the sandflies were actually derived from the leishmania in the dogs, flies (*P. intermedius*) thus infected were emulsified and inoculated intraperitoneally into hamsters (*Cricetus cricetus*). Of two hamsters subjected to several such injections one developed a generalized leishmania infection. *C. M. W.*

DAVIES (Arthur) & WINGFIELD (Alec). **Agranulocytosis in Kala-Azar and Use of Adrenalin.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. May 27. Vol. 34. No. 6. pp. 421–428. [23 refs.]

In describing a case of kala azar in an Indian seaman in London, where the complication of agranulocytosis occurred, the procedure of diagnosis by gland puncture as compared with spleen, liver and sternum puncture is discussed. The authors point out that in a limited series of cases in which they have carried out puncture of lymphatic glands they have been uniformly successful in finding leishmania by this means. As recommended by KIRK and SATI [this *Bulletin*, 1940, Vol. 37, p. 771], the glands most easily dealt with are those of the lower superficial inguinal group. The gland selected is immobilized between the finger and thumb and punctured with a dry needle into which the gland fluid readily passes. The fluid is then blown on to a slide for film making.

The case of kala azar reported is exceptional in that after the administration of 2·6 grammes of neostibosan in twelve days, during which the temperature fell and improvement occurred, the complication of agranulocytosis supervened. The temperature rose and the blood showed severe granulocytopenia. Treatment with nucleinic

acid intravenously, pentnucleotide intramuscularly and blood transfusion was carried out with little improvement. Adrenalin [presumably 1 in 1,000] 15 minims was injected subcutaneously. This produced an increase in the white cell count. In view of this response adrenalin was given frequently during the next week. Complete recovery occurred. No further antimony treatment was required as it appeared that the attack of agranulocytosis had had a curative action on the kala azar. *C. M. W.*

Andreu Urra (J.), Regli (E.) & Andreu Urra (F.). La medula ósea en el kala-azar del adulto. [**The Bone Marrow in Kala Azar of the Adult.**]—*Rev. Clín. Española.* Madrid. 1940. July 1. Vol. 1. No. 1. pp. 25–28. With 8 figs. [15 refs.] French summary p. 27.

Writing of kala azar in Spain, the authors advocate sternal puncture as a diagnostic procedure preferable to other methods. It is stated that the presence of undoubted leishmania within red blood corpuscles indicates the existence of a developmental cycle in these cells. The microphotographs purporting to illustrate this are, however, quite unconvincing.

The bone marrow changes brought about by the infection indicate a regenerative reaction of the normoblastic type and an inhibition of the myeloid cells. [See also this *Bulletin*, 1939, Vol. 36, p. 1,030; 1940, Vol. 37, pp. 349, 772, 877.] *C. M. W.*

Cook (A. Bramwell). **Kala-Azar. Report of a Case in New Zealand.**—*New Zealand Med. Jl.* 1941. Feb. Vol. 40. No. 215. pp. 53–54.

The case reported is that of an Indian seaman from Calcutta who was admitted to hospital in New Zealand for fever associated with enlargement of the spleen. Kala azar was suspected and leishmania were demonstrated by splenic puncture. The case is reported in order to call attention to the possible occurrence of the disease in lascars who may be invalided in New Zealand. The case responded well to intravenous injections of tartar emetic. *C. M. W.*

Kirk (R.) & Sati (Mohammed Hamad). **The Use of Certain Aromatic Diamidines in the Treatment of Kala-Azar.**—*Ann. Trop. Med. & Parasit.* 1940. Dec. 31. Vol. 34. Nos. 3 & 4. pp. 181–197. With 1 fig. [20 refs.]

In a previous paper the authors referred to 28 cases of kala azar in the Sudan which were treated with 4 : 4′-diamidino stilbene [see this *Bulletin*, 1941, Vol. 38, p. 260]. Details of 8 of these cases were given. Two had died and six had remained in good health for four months after discharge from hospital. It is now pointed out that the six cases are still in good health after a further two months' observation. In the previous paper it was noted that the treatment of the remaining 20 cases had not then been completed. It is now stated that of these 20 patients two died, while the remaining 18 have remained in good health for periods up to 6–7 months. This result is eminently satisfactory when it is realized that in the majority of cases one or more of the usual complications, including cancrum oris, occurred. One additional case is mentioned, in which two courses of

neostibosan and three of tartar emetic failed to bring about a cure. When the diamidino stilbene was administered an immediate response, followed by apparently complete recovery, occurred. A series of 13 cases were treated with an allied drug, 4 : 4′-diamidino diphenoxy pentane, in the same doses and by the same method of administration [see also this *Bulletin*, 1941, Vol. 38, p. 261]. There were three deaths, nine immediate recoveries and one doubtful recovery. A further two cases were treated with another drug, 4 : 4′-diamidino diphenoxy propane. Of these one died and the other recovered.

In all the above cases, with one exception in which intramuscular administration was employed, the drugs were given intravenously in a solution of 10 mgm. in 10 cc. of distilled water. The individual doses varied from 1 to 2·6 mgm. and the total quantity administered from 0·75–4·9 gm. With these drugs minor toxic symptoms were not infrequently observed but in two cases treated with 4 : 4′-diamidino diphenoxy pentane the toxic symptoms were serious. Nevertheless administration of the drug was continued in these cases with no further reactions. Of the 44 patients treated with one or other of these drugs, 8 died, but of these 5 were *in extremis* when brought to hospital for treatment. The number of cases is too low to admit of a comparison of the effectiveness of the drugs to be made. There is no doubt, however, that, compared with the results obtained in the Sudan by treatment with antimonials, the results with the new drugs are good. In a note to the paper by the Editors it is stated that the first author had sent information regarding the cure of two cases of espundia and two cases of antimony-resistant kala azar by 4 : 4′-diamidino stilbene. *C. M. W.*

Napier (L. Everard) & Sen (G. N.). **Diamidino-Stilbene in the Treatment of Kala-Azar.**—*Indian Med. Gaz.* 1940. Dec. Vol. 75. No. 12. pp. 720–725. With 3 charts.

The paper is a preliminary account of the treatment of eight cases of kala azar at the hospital of the School of Tropical Medicine, Calcutta, with diamidino stilbene. Initial intravenous doses of 0·001 gramme per kilo. of body weight were given. In most cases this dose was well tolerated but the patients became flushed, had a burning sensation all over the chest and abdomen and slight dyspnoea. These sensations, however, passed off fairly rapidly. In a few instances the ill-effects were more disturbing. The dose of the drug given daily was increased slowly, usually by 0·01 gramme till a dose of 0·002 gramme per kilo. of body weight was reached. Subsequently the maximum dose was fixed at 0·001 gramme per pound of body weight. The initial dose was then 0·05 gramme (if this was not more than two-thirds of the maximum dose) and this was increased by 0·01 gramme till after 8, 10 or 12 injections the maximum dose was reached. When the ill-effects were exaggerated relief was obtained by the administration of adrenalin. The clinical progress of the eight cases which underwent a full course was extremely satisfactory and it is expected that most of them are cured. With further experience it may be possible to eliminate the serious symptoms by administration of adrenalin, smaller individual doses or shorter courses. It is noted that two cases of oriental sore reacted badly to a single injection, both becoming unconscious. Another case of post-kala azar dermal leishmaniasis had shown distinct improvement

after 20 injections totalling 0·950 gramme. The general conclusion is that the drug is an effective therapeutic agent in the treatment of kala azar. *C. M. W.*

Wang (C. W.) & Chung (Huei-Lan). **Further Observations on Neostibosan in the Treatment of Kala-Azar in Chinese Hamsters with Especial Reference to the Development of Immunity in Hamsters cured of the Infection.**—*Chinese Med. Jl.* 1940. Dec. Vol. 58. No. 6. pp. 601–611. [16 refs.]

In a previous communication [this *Bulletin*, 1938, Vol. 35, p. 871] it was shown that 50 per cent. of Chinese hamsters experimentally infected with *Leishmania donovani* could be cured by administration of a total dosage of 5 to 7 grammes of neostibosan per kilo. of body weight. It was also shown that a group of apparently cured hamsters were immune to further inoculation, but as freedom from infection of the apparently cured animals had not been proved it was possible that at the time of the second inoculation a latent infection existed.

In the present paper further experiments along the same lines are described. Treatment in three sets of infected hamsters showed that a total dosage of 20 grammes of neostibosan per kilo. of body weight produced an actual cure rate of only 47·1 per cent. The proof of cure was the failure to discover leishmania in smears of the organs and the failure of hamsters inoculated with emulsion of spleen and liver to become infected. The dosage of neostibosan used in these experiments was actually 400 times as large as the dosage per kilogramme required to bring about cure in about 90 per cent. of human beings. As regards immunity after cure, complete disappearance of parasites was proved by removal by biopsy of a portion of the spleen and inoculating this into hamsters. If these did not become infected it was concluded that absolute cure had occurred. Four such hamsters were re-inoculated. Two months later they were killed and inoculations of spleen and liver into other hamsters was made. The result was that the re-inoculation had produced no infection in any of the four animals. *C. M. W.*

Brahmachari (U. N.). **Note on the History of the Treatment of Kala-Azar with Urea Stibamine.**—*Jl. Trop. Med. & Hyg.* 1941. June 3. Vol. 44. No. 11. pp. 67–71. With 1 fig. & 1 chart. [51 refs.]

Sallam (Hamed). **Skin Leishmaniasis in Minia District.**—*Laboratory & Med. Progress.*, Cairo. 1940. Nov. Vol. 1. No. 2. pp. 164–165. With 1 fig.

Skin lesions due to leishmania infection are very common in the Minia province of Egypt about 150 miles due south of Cairo. The patients are mainly farmers who live in villages. Their age is generally about 19 to 20 years, but all ages may be affected. Lesions in an infant and in a man of 70 have been seen. Generally the ulcers are multiple on the face, hands, forearms and legs. Occasionally they occur on the thighs, head and chest. The initial lesion is a papule which with increase in size becomes eroded to form an ulcer. This may spread at the edges to cover a wide area, while healing at the centre. In some cases there is a resemblance to lupus vulgaris. The healed part may break down again into small ulcers. Cicatrization

may be so severe as to cause deformities, especially near joints such as the elbow. In old neglected cases massive warty growths may occur—the verrucose type of Ferguson and Richards. Most of the cases respond quickly to tartar emetic, the course being 20 intravenous injections of 2 grains each. A 1 per cent. tartar emetic ointment in vaseline may be extremely useful. *C. M. W.*

Senekji (H. A.) & Beattie (C. P.). **Artificial Infection and Immunization of Man with Cultures of** *Leishmania tropica.*—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. May 27. Vol. 34. No. 6. pp. 415–419.

The authors describe the results of the inoculation of 227 persons in Bagdad with suspensions of the cultural forms of *Leishmania tropica* with the object of producing a protective immunity. The inoculum was arranged to contain twenty million leptomonads per cc. and a dose of 0·15 cc. was given intracutaneously to each individual on the front of the thigh. Of 200 cases which it was possible to follow 198 developed oriental sore at the site of inoculation in an average of two to four weeks in adults and about 2 months in children. The two cases which failed to respond to the first injection responded to a second. It was also shown that a second injection carried out on cases before the sore resulting from the first inoculation had healed developed a second sore. A similar result was obtained by the inoculation of persons with an unhealed naturally contracted sore. On the other hand, no sore developed in persons inoculated after complete healing had taken place. The high percentage of positive results is attributed by the authors to the carrying out of the inoculations intracutaneously with rich suspensions of flagellates. Both young and old cultures were employed and both gave equally good results. *C. M. W.*

Templeton (H. J.). **Cutaneous Leishmaniasis, Experimentally Produced.**—*California & Western Med.* 1941. Feb. Vol. 54. No. 2. pp. 70–71. With 2 figs.

The case reported is that of a woman who went to the U.S.A. from Beirut, Syria, where Dr. Berberian had inoculated her in the skin of the thigh with cultures of *Leishmania tropica*. Four months after inoculation a papule developed. This increased in size and finally broke down to form an ulcer measuring about one inch by half an inch. Healing eventually occurred, the total duration being seventeen months. Dr. Berberian has for some time practised protective inoculations in Beirut [this *Bulletin*, 1939, Vol. 36, p. 1035].

C. M. W.

Orsini (Olyntho). Leishmaniose em Minas Geraes. [**Leishmaniasis in Minas Geraes.**]—*Brasil-Medico.* 1940. Nov. 16. Vol. 54. No. 46. pp. 762–766. With 1 chart. [19 refs.]

Muco-cutaneous leishmaniasis is a problem of increasing importance in Minas, Brazil, and is one which urgently demands the attention of the Director of Public Health. In the north-east particularly the incidence is so high that it constitutes a veritable calamity. From 1915 to 1939 at the hospital in Bello Horizonte 238 cases were seen.

Of these, 223 were in men and 15 in women. The ages of the patients varied from 10 years to 101 years, the greatest incidence being in the age period 25 to 45. The duration of the disease in the cases coming to hospital varied from four months to four years. Though in some of the cases there were only cutaneous lesions, in the majority there was a mixed mucosal and cutaneous infection. In Minas the district most involved is in the north-east along the Rio Doce, but cases occur in all parts of the province. It would appear that the disease entered Brazil from Peru and Bolivia. Bahia and São Paulo were first invaded, the disease spreading finally to Minas, where it is at present a serious economic problem. *C. M. W.*

MAZZA (Salvador) & CORNEJO (Andres). Ensayos de atebrina en leishmaniosis tegumentaria americana. [**Atebrin Trials in American Cutaneous Leishmaniasis.**]—*Prensa Méd. Argentina.* 1940. Aug. 21. Vol. 27. No. 34. 7 pp. With 2 figs.

Seeing the announcement of FLARER of Catania that oriental sore was curable by the infiltration of the lesion with solutions of atebrin [see this *Bulletin*, 1939, Vol. 36, p. 454], the authors have tried the treatment in a case of S. American leishmaniasis in which a single sore alone existed. Infiltration of the sore was carried out with 5 cc. of a 10 per cent. solution of atebrin and at the same time three tablets were given orally each day for seven days. Complete healing of the sore had occurred in fifteen days. The good result of this treatment of the cutaneous lesions was not obtained when atebrin was employed for mucosal lesions, which failed to respond. For them combined fouadin and yatren medication remains the best. *C. M. W.*

CHOLERA.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

In the Annual Report of the Eastern Bureau of the League of Nations (p. 578) it is stated that the mortality from cholera in British India has shown a tendency to decline in the last 30 years, but that there is now a tendency for cholera to persist in inter-epidemic periods. It is generally accepted that high relative humidity with high temperature and intermittent rain provides the most suitable conditions for the development of epidemics. MAKAND (p. 579) gives information on the epidemiology of cholera in the Central Provinces of India, and in Berar.

HUANG *et al.* (p. 579) give details of the preparation of agar medium for the growth of *V. cholerae*, in which previously used agar is employed after being washed to eliminate growth-inhibiting substances remaining from previous cultures. PASRICHA *et al.* (p. 580) have shown that if faeces are highly diluted before plating, more numerous colonies of pathogenic organisms are obtained than by any direct plating method.

LINTON (p. 580) discusses the complex subject of the identification, chemical composition, sugar reactions, haemolytic action and antigenic reactive properties of *V. cholerae*, concluding that further study is called for.

Basu *et al.* (p. 581) have studied the substances which diffuse into a cellophane bag containing sterile salt solution and immersed in a fluid culture of *V. cholerae* for 5 days.

Chatterjee (p. 582) discusses the histopathological changes in the kidney in cholera. He ascribes to a histamine-like substance most of the congestive changes found and considers that the morphological changes are probably in some way connected with a hypersensitive state in the course of an infection.

Malik and Pasricha (p. 582) describe methods for estimating the chemical constituents of small quantities of blood in cholera. They (p. 583) give the results of their investigations by this method.

Chatterjee and Sarkar (p. 583) discuss the chemical composition of the blood in the condition of dehydration which occurs in cholera, pointing out the resemblances between this condition and that of shock. Földes (p. 583) gives details of a glass vessel used, with varying proportions of chloroform and benzene, to determine the specific gravity of blood and body fluids.

Ghosh and Chakraborty (p. 585) have determined the chemical composition of the stools of cholera patients. All are highly alkaline, and this elimination of alkaline base and chloride leads to acidosis and a disturbance of osmotic balance, to which may be due the suppression of urine which occurs.

Ying (p. 585) has found, as a result of an investigation of 200 cases of cholera, that although in 98 per cent. the date of the last positive culture is two weeks after the onset of the disease, there are a few cases in which positive cultures may be obtained in the fourth week. Generally speaking, cholera patients should be isolated for two weeks from the onset or for at least one week from the beginning of convalescence.

Krueger and Scribner (p. 586) have written a review of the literature on bacteriophage.

Cataldi (p. 586) describes an agar-liquefying vibrio isolated from activated sludge. *C. W.*

League of Nations. Health Organisation. Eastern Bureau, Singapore. Annual Report for 1940. pp. 37–54. With 16 graphs & 2 maps.—**(D) Cholera (General). (E) Cholera in Countries. (F) Cholera in Sea and Air Ports.**

The report treats the subject of cholera under the three headings: General, cholera in countries and cholera in sea and air ports.

(A) *Cholera (General).*—Endemic foci of cholera are being established for China as well as for British India. The National Health Administration of China put forward a scheme for the prevention and control of cholera epidemics which, with modifications, could be made to suit all tropical countries. This scheme is given in some detail.

(B) *Cholera in countries.*—In British India, judging from the figures of five-year periods from 1910–1939, the tendency is for the mortality to decline. Another tendency is noted, which is for epidemic characteristics with freedom for the rest of the year to be succeeded by endemic cholera persistent throughout the year. An El Tor epidemic in the island of Celebes has attracted much attention because the El Tor vibrio is not generally regarded as one giving rise to epidemics. It is mentioned in this report that "during the period

16th June to 27th July a further eight (8) cases of El Tor infection were notified from Celebes of which five (5) were fatal." The high mortality of this infection resembles that of true cholera.

(C) *Cholera in sea and air ports.*—It seems to be generally accepted that " the association of high relative humidity with high temperature, accompanied by intermittent rains " represents the most favourable conditions for the development of the disease in epidemic form. What has been worked out for British India should apply generally to Eastern ports and enable public health authorities to make forecasts of probable epidemic prevalence. *W. F. Harvey.*

Central Provinces & Berar. Annual Report of the Public Health Department for the Year 1939 [Makand (S. N.), Director of Public Health]. pp. 15–17. With 1 chart.—**Cholera.**

In the chapter on the epidemiology of cholera details are given, district by district, of the first cases of cholera for the season and some of the circumstances attending their appearance. Cases and deaths are all carefully recorded. Together with this annual and formal presentation there is published a useful graph of the seasonal rise and fall of cholera as shown by the number of recorded deaths month by month throughout the year. The peak numbers, 335, 479 and 361 are reached in the months August, September and October respectively. Among the chief preventive measures taken were: anticholera inoculations, disinfection of wells or water supplies and distribution of Tomb's cholera mixture. *W. F. H.*

Huang (Y. W.), Shen (T. H.) & Tang (F. F.). **A Note on the Re-Utilization of Used Agar-Agar as an Emergency Culture Medium.**—*Chinese Med. Jl.* 1941. Feb. Vol. 59. No. 2. pp. 176–178. [Summary appears also in *Bulletin of Hygiene.*]

Agar-agar is an extract of the seaweed *Gelidium corneum* and under present circumstances it is not easy to obtain supplies. The authors have experimented to find out whether it could not be used more than once. Their investigations led them to conclude that poor growths or failure of bacteria to grow on used medium sterilized were due not so much to lack of growth-promoting material as to inhibiting substances left over from previous cultivation. They, therefore, cut the used and resolidified agar into thin slices, placed them in covered bamboo baskets and the baskets into a running stream for 24–48 hours, for thorough washing. Better results were thereby obtained, but repeated autoclaving—14 or 15 lb. pressure sterilizations—gradually removes the property of solidifying on cooling, but by the addition of fresh agar, 1 part to 2 of washed agar, this was overcome. The authors now use the following formula:—

Washed agar-agar (3 per cent.)	8,000 gm. (containing 240 gm. dry agar)
Fresh agar-agar	120 gm.
Sodium chloride	40 gm.
Sodium carbonate	25 gm.
Liver digest broth	2,000 cc.
Meat infusion broth	2,000 cc.

" Sodium carbonate was added to neutralize the acidity which is apt to run very high after the agar was washed. Liver digest and meat infusion broth were used to supply peptone and other essential factors."

Repeated growth of the enterica group and of *V. cholerae* has been obtained on this, without the production of any recognizable change in morphology, cultural characteristics, serological reactions or colony formation. It is good as an emergency medium for producing vaccines. *H. H. S.*

PASRICHA (C. L.), PANJA (G.) & PAUL (B. M.). **A 'Dilution Method' for the Isolation of Pathogenic Bacteria from Faeces.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 323–325.

By dilution of a stool before plating more numerous colonies of the pathogenic organisms sought for were obtained than by any direct plating method. The exact dilution to be used is determined by experience and it was found to be much better to make the first dilution with half or one cubic centimetre of stool than with small quantities such as loopfuls. A suspension is made of 0·5 cc. stool in 4·5 cc. broth or in sterilized tap water of *p*H 7·4 and from this 10-fold dilution further 10-fold dilutions are made up to 1 in 100,000,000 or more. From the 4 highest dilutions amounts of 0·5 cc. are plated immediately after preparation in 5-inch Petri dishes. "The inoculum is spread by a combination of rotary and tilting movement."

As explanation of the better results obtained by dilution it is suggested that either other bacteria exert an inhibiting influence on the pathogenic organisms, which is diminished by good separation of colonies, or the clumps of the pathogenic organisms are broken up in the course of dilution to give more numerous separate colonies. The latter explanation is the one preferred. "Results obtained indicate that this method is of considerable value in the isolation of pathogenic bacteria." *W. F. H.*

LINTON (R. W.). **The Chemistry and Serology of the Vibrios.**—*Bact. Reviews.* 1940. Dec. Vol. 4. No. 4. pp. 261–319. [169 refs.]

This review deals critically and controversially with the subject of the so-called "true" cholera vibrio and the vibrio group in general. Obviously we are mainly concerned with deciding which vibrio is pathogenic. By a series of steps it may be said that agreement has been reached to call that organism the true cholera vibrio which (1) ferments mannose and sucrose but not arabinose, (2) does not haemolyse goat erythrocytes and (3) agglutinates with O-group I serum. But no single one of these characteristics suffices to pick out the cholera vibrio; it requires all three to do so with certainty. This seems to the author "difficult to reconcile with the orthodox teaching that the cause of cholera is a distinct entity utterly unrelated to other vibrios." He himself would not insist on such complete separation of the vibrio-cause of cholera from vibrios of other groups. His own work is very well known and has resulted in finding a chemical composition for vibrios which when grouped gives six combinations only of 3 different carbohydrates and 2 proteins. One polysaccharide and one protein are commonly obtainable from each strain of vibrio and if exceptions to this rule occur it is invariably found that the strain is undergoing dissociation. Other authors have attacked the problem from their own particular point of view. Bruce WHITE concluded that each type of vibrio growth (S, R, and ρ) had its own

characteristic complex of saccharides :—in the S form α, β, γ, δ; in the R form β, γ, δ, and in the ρ form γ, δ. " Type α was dominant in the smooth form, β in the rough and δ in the rho, and the loss of these dominant substances from the S and R forms led to the domination by another of the substances which was previously present, but masked." Another attempt to classify vibrios is that of HEIBERG in which six groups also emerge according to power of producing acid in one or more of the sugars mannose, arabinose and sucrose.

The discovery of the haemolytic El Tor vibrio having serological identity with the non-haemolytic cholera vibrio is now an old story, but has recurred as a problem in connexion with the investigation of new El Tor strains and the haemolytic epidemic strain known as *V. celebes*. van LOGHEM described haemolytic action by *V. cholerae* as haemo digestion and not true haemolysis by an exotoxin. He posed the questions which are still unanswered : " Can a non-haemolytic true vibrio become haemolytic ? and can a haemolytic strain cause cholera ? "

A departure from pure chemical, fermentation and haemolytic characters is made with the resort to specific antigenic reactive properties and these are probably the most important of all for the differentiation of the possible vibrio pathogens. The scheme of GARDNER and VENKATRAMAN is almost universally adopted and depends on the definition of the cholera group as those vibrios which are biochemically and bacteriologically similar to *V. cholerae* and possess a common " H " antigen. The first subdivision of this group is the O-group I which yields (1) the non-haemolytic (goat cells) cholera vibrios of original (Inaba), variant (Ogawa) and middle (Hikojima) types and (2) the haemolytic El Tor vibrios. The second subdivision of the main group includes O-groups II, III, IV, V, VI and individual races (mostly haemolytic) among which are found " paracholera, cholera-like and some El Tor vibrios." The work of many other authors is taken up critically in this review, which should be consulted for the detail. DE MOOR came to the opinion that " Asiatic cholera should be considered a disease in the same sense as bacillary dysentery, in which the same or a very similar disease may be due to bacteriologically different organisms."

The author's own conclusions evidently tend towards the rejection of too rigidly selective a definition for the cholera vibrio, and he calls for further study of the problem. " The application of the concepts of somatic and flagellar antigens has defined rather than solved the problem of cholera etiology. The results obtained in the study of dissociation may prove of value when applied to epidemiology or it may be found that the variants are merely abnormalities produced in the laboratory. These larger problems as well as lesser ones in the study of haemolytic power, metabolism and toxigenicity urgently call for study, to the end that cholera may be still further reduced and confined to its Asiatic home." *W. F. H.*

BASU (Charuchandra), CHAUDHURY (Anilkrishna) & BASU (Ramendranath). **Study of Fluid Diffusates obtained by cultivating *Vibrio cholerae*. A Preliminary Note.**—*Calcutta Med. Jl.* 1940. Sept. Vol. 37. No. 9. pp. 571–576. With 1 fig.

The dialysing apparatus used in these experiments consisted of a cellophane or collodion bag containing sterile salt solution immersed

in a growing culture of *V. cholerae*. The culture medium was a Difco proteose peptone solution of *p*H 7·8. After five days' incubation the contents of the bag, the "diffusate", were filtered through an L3 Chamberland candle and put through various tests to determine their nature. Intraperitoneal injection of the filtrate in doses of 5 cc. was well tolerated by the guineapig, but a dose of 1 cc. in the rat was followed by restlessness, cramps, paresis and signs of imminent death. These remarkable symptoms in the rat lasted only 10 to 12 hours and the animal had completely recovered in 24 hours. The remaining tests of the diffusate were chemical and immunological: It "contains carbohydrate substances and practically no protein"; "gives rise to agglutinin and precipitin in the blood of the rabbit and protects it against injection of lethal doses of *Vibrio cholerae*"; it furnishes an antiserum which will prevent the development of the remarkable symptoms noted in the rat and is thermostable.

Neither chemical nor biological tests give any indication that the diffusate was a histamine-like substance. *W. F. H.*

CHATTERJEE (Hemendra Nath). **Histopathology of the Kidney in Cholera.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Jan. 31. Vol. 34. No. 4. pp. 333–342. With 3 figs. on 2 plates. [44 refs.]

The histopathological changes in the kidney in cholera are surprisingly inconstant and inconspicuous. In this study, 13 cases of cholera with uraemia and 25 cases without uraemia have been examined *post mortem*. As might be expected the changes in the non-uraemic kidneys are much less marked than in the uraemic. These changes are very shortly described as: congestion of capillaries in glomeruli and medulla, swelling of the glomeruli so as to fill the capsule, hyaline fibrillation of the basement membrane, practically complete absence of the inflammatory cellular features of a glomerulonephritis. As the changes in the kidney are non-inflammatory it is not to be wondered at that recovery of renal function is complete if the cholera attack itself is recovered from. Most of the congestive change in the kidney is ascribed to the action of a histamine-like substance and the anuria to deficient blood pressure. Although it may be contended that cholera is too acute for the changes of glomerulonephritis to take place, the evidence, according to the author, "tends to support the explanation that the morphological changes that occur in the kidney . . . are in some way connected with a hypersensitive state in the course of an infection." *W. F. H.*

MALIK (K. S.) & PASRICHA (C. L.). **The Blood in Cholera. Part I. Technical Methods.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 291–299.

Methods are here described for estimating the chemical constituents with small quantities of cholera blood. The blood was oxalated with 3 mgm. potassium oxalate for each cc. of blood and tubes were prepared with the dried oxalate to receive 4, 5 or 6 cc. of blood according to the circumstances of the case. It takes about 4 cc. blood to determine cell volume and fractional portions of a cubic centimetre for the other estimations. These other estimations were: sugar, haemoglobin,

moisture, urea and chlorides of whole blood ; and sugar, total non-fibrin nitrogen, globulin, moisture, chlorides, non-protein nitrogen and inorganic phosphate of plasma. Detailed descriptions of the micro-methods are given. *W. F. H.*

PASRICHA (C. L.) & MALIK (K. S.). **The Blood in Cholera. Part II. Certain Chemical Constituents.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 301–307.

In this part of the investigation the results obtained by the methods described in the first part are given. Altogether 17 cholera patients, all in the acute stage of the disease, were examined before the administration of any saline transfusion. One patient died on the first day of the disease, all the rest recovered rapidly. The records show wide variations in individual cases but "suggest that in the acute stage of cholera there is : (1) An increase in the cell volume. (2) An increase in the haemoglobin percentage. This increase is directly correlated with the cell volume. (3) A decrease in moisture content of the blood and plasma but this decrease is not marked in the acute stage of the disease. (4) An appreciable increase in the urea and non-protein nitrogen. (5) An appreciable increase in the total plasma proteins, fibrin and globulin fractions . . . ." (6) An increase in the organic phosphates. (7) An appreciable increase in the glucose concentration in the blood and the plasma. (8) A diminution in the concentration of the sodium chloride in the blood and in the plasma, but this diminution is not marked." *W. F. H.*

CHATTERJEE (Hemendra Nath) & SARKAR (Jamini). **Biochemical Study of the Blood of Cholera Patients.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 379–386. [27 refs.]

It must be remembered that in cholera there occurs a great concentration of the blood due to dehydration. In consequence of this it is essential not merely to study the chemical composition of the blood, but also to consider the effect on this of the three factors : "the specific gravity of the blood, the total number of red cells and the corpuscular volume." The main findings in this research were : (1) diminution of sodium content and increase in potassium content ; (2) lowering of serum calcium, but increase during clinical improvement even without its therapeutic replacement ; (3) diminution of serum chloride but proportionately less than that of sodium ; (4) decrease in blood sugar in most cases ; (5) increase of urea and non-protein nitrogen.

One of the most important features of cholera is acidosis and there is also increase of inorganic phosphates. Acidosis, however, is similarly found in shock with its marked decrease in alkali reserve. Other changes found in cholera, as in the serum electrolytes and the hypoglycaemia, have also been observed in shock. *W. F. H.*

FÖLDES (Francis). **A New Method for determining Specific Gravity of Blood and Body Fluids.**—*Jl. Lab. & Clin. Med.* 1941. May. Vol. 26. No. 8. pp. 1370–1373. With 2 figs.

The method is a modification of Hammerschlag's original method of determining the specific gravity of blood by means of a mixture of

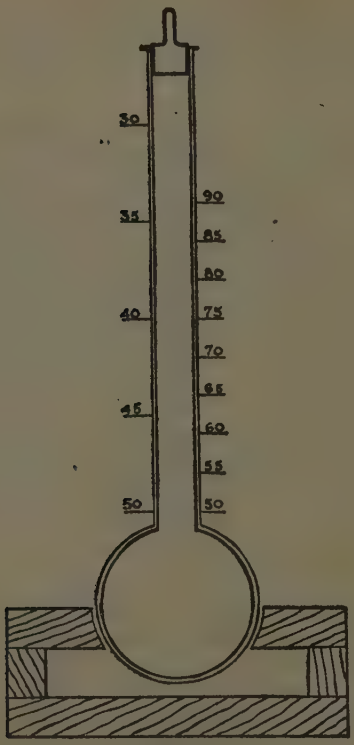

Fig. 1.

[Reproduced from the *Journal of Laboratory and Clinical Medicine*.

chloroform and benzene in which a drop of the blood floats at the centre. It depends on the use of a glass vessel which is bulbous below and cylindrical above [see figure]. The cylinder bears the base mark 1·050 close above the bulb and this represents the point to which 25 cc. of a chloroform-benzene mixture of this specific gravity is filled. Marks succeed one another from this point on the cylinder of 1·050, 1·045, 1·040 . . . 1·030 on the one side and 1·050, 1·055, 1·060 . . . 1·090 on the other. These points show the amount of rise of fluid in the gradation of the instrument according as benzene (S.G. 0·884) or chloroform (S.G. 1·476) is added to the 1·050 mixture to obtain the several specific gravities, which must obviously fall in the one case and rise in the other. To use the instrument: fluid of 1·050 specific gravity is filled to the 1·050 mark and a drop of blood is added to it with a teated pipette. If the specific gravity of the blood exceeds this figure, the drop will sink and chloroform is added in small quantities until it comes to float at the centre of the mixture contained in the globular part of the vessel. If on the other hand the specific

gravity is less than 1·050 the drop will remain on the surface and it will be necessary to add benzene until it floats in the middle. In order to obtain graduations of the instrument 1·055 and 1·045, that is to say amounts of chloroform or benzene to be added to the original 25 cc. of 1·050 specific gravity, the two equations are used: (1) $25\times 1{\cdot}050+1{\cdot}476x=1{\cdot}055\times(25+x)$ and (2) $25\times 1{\cdot}050+0{\cdot}884y=1{\cdot}045\times(25+y)$ respectively, where x (chloroform)=0·297 cc. and y (benzene)=0·776 cc. With the necessary substitutions in the equations the volume additions for rising specific gravities 1·060, 1·065 . . . and falling specific gravities 1·040, 1·035 . . . may be calculated. Similar vessels may be prepared for other ranges of rising and falling specific gravities. *W. F. H.*

Ghosh (H.) & Chakraborty (R. K.). **Chemical Constituents of the Stool of Cholera Patients.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 309–313.

All these experiments were made with fresh samples of stools and the methods of determination of the chemical constituents are given in some detail together with the data obtained from examination of 31 cases. The conclusions reached are that:—"All cholera stools are highly alkaline and it seems positive that alkaline reaction of the medium is distinctly favourable to the formation of cholera toxin. This is also corroborated by the fact that *Vibrio cholerae* grow abundantly in highly alkaline medium. Elimination of alkaline base and chlorides is also considerable. This leads to acidosis and disturbs the osmotic balance. The suppression of urine may be partially due to the disturbance of this osmotic balance." *W. F. H.*

Ying (Y. Y.). **The Persistence of Vibrios in Cholera Patients. A Study of Two Hundred Cases.**—*Chinese Med. Jl.* 1940. Nov. Vol. 58. No. 5. pp. 595–596.

A large series of cases of epidemic cholera—200 in all—have been examined to determine "(1) How long will the organism remain in the intestinal tract of the patient? (2) When can a case of cholera be discharged without risk to the community?" The figures given supply much of the answer to these important questions and are set out for weekly periods: they refer to the bacteriological isolation and recognition of the *V. cholerae* by cultural, morphological, chemical and agglutination testing. Three separate headings make up the short table given: "(1) The date of the last positive culture (200 cases). (2) The date of the first negative culture (200 cases). (3) The date of the first negative culture, counting from the time of clinical convalescence (subsidence of acute symptoms) 193 cases, average duration of acute symptoms 4·5 days."

Percentages.

	1st week.	2nd week	3rd week	4th week
(1)	76·5	21·5	1·5	0·5
(2)	16	75	8	1
(3)	88·1	9·3	—	2·6

It is evident that in this series 98 per cent. of the cholera stools showed their last positive culture of cholera vibrios by the second week, but that a few still gave positive cultures into the third and even the fourth week. A scrutiny of these figures justifies the observation that " it is a dangerous practice to send away active cases after saline injections, or after a few days of hospitalization, or as soon as acute symptoms abate. Generally speaking in the absence of laboratory controls cholera patients should be isolated for two weeks from the date of onset or at least one week from the beginning of convalescence."

W. F. H.

Krueger (Albert Paul) & Scribner (E. Jane). **The Bacteriophage. Its Nature and its Therapeutic Use.**—*Jl. Amer. Med. Assoc.* 1941. May 10 & 17. Vol. 116. Nos. 19 & 20. pp. 2160–2167; 2269–2277. With 3 figs. [152 refs.]

This is a long article in which a mass of literature on bacteriophage is reviewed. The subject is dealt with from the points of view of the nature of phage and the experimental and the clinical evidence of its usefulness in treatment. To readers of this *Bulletin* the section dealing with choleraphage will be of interest; most of the papers reviewed have been abstracted before, but the article gives a readable and useful résumé of the subject. *C. W.*

Cataldi (Maria S.). Una nueva bacteria licuante del agar. [**A New Agar-liquefying Bacterium.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1940. June. Vol. 9. No. 3. pp. 366–377. With 4 figs. [12 refs.] English summary.

It was long thought that agar was a carbohydrate incapable of being liquefied by bacteria and it was not till 1902 that this was proved not to be the case with the discovery of *Bacterium gelaticus*. Several agar-liquefying bacteria are now known. The present organism, isolated from activated sludge, is a new species for which the name *Vibrio agarlyticus* is suggested. It is a highly motile, Gram-negative, comma bacillus with single polar flagellum, capable of growing aerobically on ordinary glucose agar at an optimum temperature of 37°C.; does not attack cellulose; gives neither a methyl red, nor a Voges Proskauer, nor an indole reaction; reduces nitrates to nitrites, and ferments many sugars but not glycerine.

W. F. H.

AMOEBIASIS AND INFECTIONS WITH OTHER INTESTINAL PROTOZOA.

Précis of Abstracts in this Section.

McMullen and Gray (p. 588) report a 10 per cent. incidence of *Entamoeba histolytica* in stools examined in Oklahoma, and give figures of the other parasites found. Reardon (p. 588) reports *E. histolytica*

in 40–44 per cent. of patients in a hospital for mental defectives in Georgia, U.S.A. Hegner *et al.* (p. 589) found *E. histolytica* in the stools of 25 per cent. of schoolchildren in Mexico, and note a distinctly familial incidence of the infection. In Toronto, however, Kuitunen-Ekbaum (p. 589) found *E. histolytica* only once in 324 persons examined.

Snyder and Meleney (p. 589) have succeeded in producing excystation of *E. histolytica* in media free from bacteria by the addition of reducing agents. Excystation will not take place unless the oxygen tension is reduced either by living bacteria or by certain chemical agents. Adler and Foner (p. 590) describe a semi-solid medium in which *E. histolytica* grows well, particularly if the medium is first inoculated with *Chromobacterium prodigiosum*.

In a series of 202 post mortem examinations of persons in New Orleans who had died as a result of accident, Faust (p. 590) found *E. histolytica* in 13 instances, in 7 of which there were associated lesions of the bowel wall. These lesions were of a mild type, and did not in any case resemble the definite amoebic ulcers reported by other workers; none of the destructive processes extended below the muscularis mucosae. The author concludes that the conception of amoebic invasion of the bowel wall must be revised to include the milder type of tissue damage now for the first time clearly demonstrated. In monkeys, Johnson (p. 591) reports that although no lesions were found in three of ten infected with *E. histolytica*, the remaining seven showed microscopic lesions containing the parasite, and concludes that this study of apparently healthy carriers gives support to the belief that it is unlikely that any infected individuals escape without some damage to the tissues.

Freeman *et al.* (p. 591) report a case of amoebiasis of the skin in a patient who had a history of recurrent dysentery for 20 years. Treatment with emetine and with zinc peroxide dressings was successful.

Beregoff-Gillow (p. 592) describes cases of ulcerative colitis which are stated to have been associated with amoebic dysentery.

La Barge (p. 592) reviews the literature on amoebiasis and liver abscess in the United States, discussing diagnosis and reviewing the results of treatment.

Liu (p. 593) reports on the seeds of *Brucea sumatrana* and of *B. javanica* in the treatment of intestinal amoebiasis, giving directions for administration and an account of the treatment of 50 cases. Results are said to be good in eliminating both the vegetative and the cystic forms of *E. histolytica*.

Rothman and Epstein (p. 594) put forward the view that *Endolimax nana*, *Entamoeba coli* and other intestinal amoebae are liable to cause ill health. This opinion was not accepted by some of the speakers in the discussion which followed the reading of the paper. Hood (p. 594) claims that *Dientamoeba fragilis* is capable of causing intestinal symptoms, and that the infection can be cured with emetine.

Yakimoff (p. 595) reports that in Russia there have been several cases of human dysentery occurring along with amoebiasis in pigs, but does not claim that correlation has been established.

Brooke (p. 595) discusses the cysts of *E. coli* which contain more than the usual eight nuclei.

NUTTER *et al.* (p. 595) describe symptoms associated with infection with *Giardia intestinalis*, of which the commonest is diarrhoea. Treatment with atebrin eliminates the parasite, and in the authors' cases put an end to the diarrhoea. *C. W.*

MCMULLEN (Donald B.) & GRAY (James K.). **The Incidence of Intestinal Parasites in Fecal Samples Collected in Eastern Oklahoma.** —*Southern Med. Jl.* 1941. Feb. Vol. 34. No. 2. pp. 177–180. With 1 fig. [10 refs.]

A survey of intestinal protozoal and helminthic infections was carried out in Oklahoma by the examination of 924 faecal specimens, most of which came from the eastern part of the State. The samples, preserved in iodine, were sent by post to the laboratory in Oklahoma City, where they were submitted to the zinc sulphate floatation method of Faust. About 60 per cent. of the specimens were positive for one or more parasites, the rural districts giving a figure about twice as great as that of the urban districts. The highest incidence was 47 per cent. for *Entamoeba coli*, while that for *E. histolytica* was 10 per cent.

The following is the complete finding in percentages, based on cysts or eggs :—*E. histolytica* 10, *E. coli* 47, *Endolimax nana* 14, *Iodamoeba bütschlii* 5, *Chilomastix mesnili* 2, *Giardia intestinalis* 5, *Necator americanus* 1, *Ascaris lumbricoides* 0·3, *Enterobius vermicularis* 0·4, *Taenia* sp. 0·2, *Hymenolepis nana* 5, *H. diminuta* 0·1.

C. M. Wenyon.

REARDON (Lucy V.). **Incidence of *Endamoeba histolytica* and Intestinal Nematodes in a Georgia State Institution.** [Research Notes.]—*Jl. Parasitology.* 1941. Feb. Vol. 27. No. 1. pp. 89–90.

A number of inmates of the State Hospital at Milledgeville, for mental defectives, were examined for *Entamoeba histolytica* and helminthic infections. General examinations were carried out in June and November 1938, while in October an examination for *Enterobius vermicularis* alone was made. Though the infection rate was high the physical condition of those examined was good, no symptoms attributable to the infections being observed. In the table reproduced here the percentage of infection is shown :—

TABLE.—*Record of positive diagnoses for intestinal parasites.*

Date	Patients examined	*Entamoeba histolytica*	*Ascaris lumbricoides*	*Necator americanus*	*Trichuris trichiura*	*Strongyloides stercoralis*	*Enterobius vermicularis*
1938	No.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
June ...	72	40	14	33	65	6	53
November ...	70	44	9	30	61	6	69
October ...	88	—	—	—	—	—	27

C. M. W.

Hegner (Robert), Beltrán (Enrique) & Hewitt (Redginal). **Human Intestinal Protozoa in Mexico.**—*Amer. Jl. Hyg.* 1940. Sept. Vol. 32. No. 2. Sect. C. pp. 27–44. [20 refs.]

——, —— & ——. Protozoarios intestinales humanos en México.—*Rev. Inst. de Salubridad y Enfermedad. Trop.* Mexico. 1940. May. Vol. 1. No. 2. pp. 151–178. [20 refs.]

The authors have carried out an intestinal protozoal survey of inhabitants of Mexico. In all, 833 individuals of different ages and social conditions were examined by a ten minutes' scrutiny of one saline and one iodine preparation of faeces, following the administration of a saline purgative. The individuals examined were school children of two districts of Mexico City and individuals in six other towns. All the usual infections were noted, with the exception of *Dientamoeba fragilis*, *Retortamonas intestinalis* and *Enteromonas hominis*, which are difficult to identify in a rapid examination such as the one which was carried out. The persons examined were classified according to race, age, sex, altitude of locality, etc., but little variation from the general result was noted. The most striking feature was the high infection rate of 25 per cent. for *Entamoeba histolytica*. Other infections were correspondingly high, with the exception of *Endolimax nana*, which was unexpectedly low. An interesting feature was the family incidence of *E. histolytica*. If one member was found infected other members were more often infected than the general incidence would indicate. *C. M. W.*

Kuitunen-Ekbaum (E.). **A Survey of Entozoa in Adults in a Toronto Hospital.**—*Canadian Med. Assoc. Jl.* 1940. Nov. Vol. 43. No. 5. pp. 451–453.

Faecal samples were examined from 324 patients in Toronto Western Hospital. One or other of the common intestinal protozoa were found in 89 of these. Only one case of *Entamoeba histolytica* infection was detected. Five cases of helminthic infection were noted. A group of 306 patients examined by the swab method showed that 30 were positive for enterobiasis. *C. M. W.*

Snyder (Thomas L.) & Meleney (Henry E.). **The Excystation of *Endamoeba histolytica* in Bacteriologically Sterile Media.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 63–73. With 2 plates.

The authors describe a method for obtaining cysts of *Entamoeba histolytica* free from living bacteria. When these cysts are suspended in various media they will not excyst unless living bacteria are added, or methods for decreasing the oxygen concentration of the medium are employed. Such methods are the addition of reducing agents, cystine or neutralized thioglycollic acid, aeration with nitrogen or extraction of oxygen by alkaline pyrogallol. Excystation was shown to occur in medium containing only inorganic salts. Continued culture of bacteria-free excysted forms has not been possible without the addition of living bacteria. It will not occur with killed bacteria. It is evident that excystation will not take place unless the oxygen tension of the medium is reduced either by living bacteria or by certain chemical agents. *C. M. W.*

ADLER (S.) & FONER (Annie). **Culture of Intestinal Protozoa.**—*Lancet.* 1941. Feb. 22. pp. 243–244.

To the list of media which have been advocated for the culture of *Entamoeba histolytica* and other intestinal protozoa the authors add yet another. It consists of a mixture of 3 per cent. agar (1 part), Locke solution (8 parts) and inactivated serum of horse, cow, goat or man (1 part). Rice starch is added and the medium tubed in 5 cc. amounts. In this semi-solid medium good growths of the amoeba are obtained all through the medium, particularly if the tubes are first inoculated with *Chromobacterium prodigiosum*. *Trichomonas hominis* and *Balantidium coli* were also grown in the medium. A mixed culture of *E. coli* and *E. histolytica* was inoculated subcutaneously to a rabbit. An abscess formed. No amoebae were seen in the pus but from the abscess wall *E. histolytica* was recovered. *C. M. W.*

FAUST (Ernest Carroll). **Amebiasis in the New Orleans Population as revealed by Autopsy Examination of Accident Cases.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 35–48. [10 refs.]

Previous attempts to obtain information about the condition of the large intestine in cases of amoebiasis free from dysenteric symptoms have consisted in the examination of hospital patients who have died from causes other than amoebic dysentery. In all cases reported in which dysentery amoebae were found in the large intestine, definite amoebic ulceration occurred. It appeared that all infections of the intestine with *Entamoeba histolytica*, including symptomless carriers, were associated with the presence of typical amoebic ulcers.

In order to throw further light on the subject, the author of the present paper examined the large intestine in 202 cases of death from accident in New Orleans, in which the autopsy was carried out within four hours of death. The contents of the large intestine were examined with and without concentration in wet iodine preparations; films of the material were made for subsequent haematoxylin staining, scrapings from any lesions present were examined, while uninjured lesions were excised and fixed for sectioning. The result was the discovery of 13 cases of *E. histolytica* infection, of which 7 showed amoebic lesions. The lesions were of three types: (1) initial pin-point ulceration, (2) shallow crater-like lesions, (3) extensive very shallow denudation of the mucosa. In no case were the definite amoebic ulcers reported by other observers encountered. None of the destructive processes extended below the muscularis mucosae, none showed leucocytic infiltration or evidence of bacterial invasion and none had fibrous repair tissue in the vicinity. In five of the cases amoebae were found in scrapings from the lesions, in two in mucus from the surface of the lesions or near by. Of the seven cases of infection in which no lesions could be detected, four showed amoebae throughout the length of the large intestine, while two revealed minimal infections as evidenced by the discovery of only a single cyst in each case. As regards the position of the lesions there was a preponderance of these in the caecum-appendix area. When cysts were discovered these belonged to different races, the diameters varying from 7μ to 16μ. The author concludes that the conception of amoebic invasion of the human bowel wall must be revised to include the milder types of tissue damage now for the first time clearly demonstrated.

In addition to *Entamoeba histolytica* various other protozoa and certain helminths were encountered. In all 42 cases of parasitic infection were met with. *C. M. W.*

JOHNSON (Carl M.). **Observations on Natural Infections of *Endamoeba histolytica* in Ateles and Rhesus Monkeys.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 49–61. With 4 figs. on 2 plates.

An examination of the faeces of a number of monkeys in Panama showed that seven local spider monkeys and four *M. rhesus* from India harboured *Entamoeba histolytica*. Only one of these, a red spider monkey, gave any clinical signs of infection. It suffered from diarrhoea, developing finally into dysentery during the 98 days of its observation. In the whole of the time free amoebae were present. Cysts were never encountered. The animal died of its infection. After death it was found that the mucosa of the large intestine was almost completely destroyed, while the submucosa revealed a diffuse amoebic invasion. The remaining monkeys appeared to be healthy carriers. They were kept under observation for periods of 40 to 623 days during which amoebae or cysts appeared to be constantly present in the stools. The ten animals were finally killed and submitted to careful post mortem examinations. Macroscopically the intestine of nine presented no abnormalities, while in one the caecal mucosa revealed a slight granulation. Microscopically, however, seven of the ten showed lesions containing *E. histolytica*. In one spider monkey and two *M. rhesus* no lesions were detected. Tests for occult blood had been carried out during life, with negative results, thus indicating that a negative blood test is no proof that lesions do not occur. The author concludes that the study gives support to the belief that it is unlikely that any infected individuals escape without some damage to the tissues. *C. M. W.*

FREEMAN (Bromley S.), SCHREK (Robert) & BROWN (Paul F.). **Amebiasis Cutis: Report of a Case.** [Abstract of paper read at Scientific Proceedings of the 40th Annual Meeting of the American Association of Pathologists and Bacteriologists, Pittsburgh, Penn., 1940, Mar. 21st & 22nd.]—*Amer. Jl. Path.* 1940. Sept. Vol. 16. No. 5. p. 704.

"A case is reported of a 48 year old laborer with a history of recurrent dysentery for 20 years. Two years prior to admission a progressive swelling and ulceration of the abdominal wall developed after a bruise with a dirty shovel. Surgical and medical treatment at various clinics did not prevail against the lesion. The patient was sent to the tumor clinic with a diagnosis of carcinoma of the abdominal wall.

"Physical examination showed an emaciated male with a foul-smelling abdominal ulcer, measuring 15 cm. in diameter, and 3·5 cm. deep. The base of the ulcer appeared to be on the peritoneum. A sinus was injected with lipiodol but revealed only a long sinus in the lateral abdominal muscles and no fistula could be demonstrated. A biopsy revealed necrotic tissue and numerous amebae in the adjacent viable tissue. The amebae contained phagocytized red blood cells, were motile in fresh smears, and could be cultivated on special

mediums. The parasites were identified as *Entameba histolytica*. Similar amebae were obtained from the feces. Bacteriological cultures of the ulcer revealed numerous types of organisms, including amebic non-hemolytic streptococci.

"Both the general condition and the ulcer improved greatly following a course of emetine and daily zinc peroxide dressings. The wound healed completely without the use of skin grafts."

BEREGOFF-GILLOW (Pauline). **Amoebic Dysentery and Ulcerative Colitis. (A Report of Seven Cases.)**—*Canadian Med. Assoc. Jl.* 1940. Dec. Vol. 43. No. 6. pp. 588–591.

The cases described are claimed to be of interest because all developed ulcerative colitis following amoebic dysentery, but none of them had a stool examination performed until two or three months after the initial complaint. Five had colostomies performed and all have recovered after prolonged treatment with high colonic irrigations of various antiseptics and proper diet with the addition of vitamins. Two cases of severe haemorrhage were treated for the first time with vitamin K.

In Case 1 *Entamoeba histolytica* was found after the patient had been suffering from acute colitis for three years. The tuberculin test was positive and a guineapig inoculated with rectal excretions died of tuberculosis in six weeks.

Case 2 commenced as an acute case of ulcerative colitis and had an ileostomy of three years standing (it is not clear from the description whether a colostomy was performed first and ileostomy later), and eventually *E. histolytica* cysts were demonstrated in the faeces after an interval of three years.

Case 3 also had an ileostomy of three years' standing and was acutely ill with pyrexia and severe anaemia. No evidence of amoebiasis was ever produced.

Case 4 was considered to have contracted amoebic dysentery in Chicago in 1935, but here again after an interval of two years no *E. histolytica* was ever demonstrated.

In the remaining three cases the evidence of a primary amoebic infection is equally uncertain.

[The reviewer is of the opinion that the clinical histories of these seven detailed cases are characteristic of acute ulcerative colitis and that the diagnosis of *E. histolytica* on verbal evidence without actual demonstration of the living organism was fallacious.]

P. H. Manson-Bahr.

LA BARGE (O. J.). **Subdiaphragmatic Abscess of Amebic Origin. A Brief Review of the Literature.**—*Rocky Mountain Med. Jl.* 1940. Dec. Vol. 37. No. 12. pp. 961–969. With 1 fig. [34 refs.]

The subtitle of this article indicates that it is itself of a review nature, and consequently the main points only will be referred to here, as the article does not lend itself to abstraction.

In 1934, CRAIG estimated that 10 per cent. or more of the population of the United States were carriers of *E. histolytica* though they presented few or no clinical symptoms. GOLDBURGH found among 120,000 admissions to the Jefferson Hospital, Philadelphia, and 3,000 autopsies there during ten years, one case only of amoebic liver

abscess; at the Philadelphia General Hospital over the same period there were five cases among 232,000 admissions and 24,000 autopsies. Nevertheless, incidence of amoebic infection among 1,060 college freshmen in Philadelphia in 1934 was 4·1 per cent. More than four-fifths of liver abscesses were in the right lobe; of 2,121 collected cases 1,792, or 84·4 per cent., were in the right lobe. Clinical symptoms usually develop in three months, or even less, after the onset of dysentery, but others may show nothing for perhaps 10 years; the onset may be acute but is more often chronic, with a low type of fever, weakness, anorexia, nausea, loss of weight, chills, and sallow subicteric complexion. There may be sharp rises of temperature if the lesion is extending rapidly or secondary infection occurs. Amoebae are found at the time in the stool in only a little over 10 per cent. of cases; in 11·3 per cent. of 3,969 collected cases. The leucocytosis present is not extreme, 15,000 per cmm. is a fair average with relative polymorphonuclear count of 78 per cent. Craig's complement fixation test is a valuable diagnostic aid in difficult or doubtful cases and X-ray is very dependable. Aspiration is not free from risk. Whipple even goes so far as to say that the dangers far outweigh the advantages. The commonest complication of subphrenic extension of an amoebic abscess of the liver is extension to the right pleural cavity. In 52 cases with complications pleural effusion was present in 31 per cent., empyema in 15, rupture into a bronchus in 13 per cent., and rupture into the pleura in a like proportion. Rapidly developing abscesses are more likely to rupture into the cavity, while those developing more slowly set up a basal pleuritis with obliteration of the cavity, and extend into the lung itself.

Emetine is preferable to open operation unless secondary infection has occurred. The prognosis, if the abscesses are multiple, is very grave, as compared with that in monolocular abscesses. Of 87 cases of single abscess the fatality was 11·4 per cent. (*i.e.* 10 cases), whereas all of twelve with multiple abscesses died. As regards the question of aspiration or open operation: of 4,780 uninfected cases treated by open operation 44·2 per cent. were fatal, whereas of 457 treated by aspiration the fatality was only 6·7 per cent., or less than one-sixth.

H. H. S.

Liu (Hsiao-Liang). *Ya Tan Tzu* (**Kho-Sam**) **in Intestinal Amebiasis.**—*Chinese Med. Jl.* 1941. Mar. Vol. 59. No. 3. pp. 263–277. [10 refs.]

Ya Tan Tzu, the seeds of *Brucea sumatrana*, or *B. javanica* are imported from Canton and Hong Kong and have long been reported to possess antidysenteric properties.

The material for study consisted of a group of 50 cases. Black seeds are selected, the shell broken and the kernel administered, the average weight of which is 0·036 gm. Only unbroken kernels should be used because the broken surface of the kernel is very bitter and possesses emetic properties when swallowed. Each is punctured in about five places with a fine needle to about 1 millimetre in depth in order to render it more easily digested. They are then put into gelatin capsules and administered one hour before, or three hours after, a meal. Strict rest in bed is necessary. Dosage of the seeds is calculated by the number of kernels.

Based upon the data of 50 cases during the last four years and four months, a ten-day course for different classes of amoebic infection has been prepared. In case of diarrhoea or nausea it is advisable to suspend treatment for a day or two and use smaller doses.

The dosage over a ten-day course works out from 20–30 seeds according to the severity of the clinical manifestations The principle being to give smaller doses in cyst-carrier and chronic cases. The dosage is calculated on the basis of 2–3 seeds per kilo. body weight. The total quantity is divided into 7 doses—one is administered daily for four days, followed by one day rest and then one every other day for three doses, but the daily dosage may be given in two divided portions. Toxic effects observed were nausea, vomiting, abdominal pain, purging and straining, but these were never severe. It is considered that the seeds are specific both for the cystic and vegetative forms of *E. histolytica*. The curative and probably curative rate for the former is 77·7 per cent. and the latter 75·6 per cent. Failures are attributed to inadequacy of dosage rather than inefficacy of the drug. Some difficulty has been experienced in assessing what should be considered a criterion of cure. Some cases were only followed up for one month, but others as long as two years. *P. M.-B.*

ROTHMAN (Maurice M.) & EPSTEIN (Harry J.). **Clinical Symptoms associated with the So-called Non-Pathogenic Ameba.**—*Jl. Amer. Med. Assoc.* 1941. Feb. 22. Vol. 116. No. 8. pp. 694–699. With 2 charts. [34 refs.]

This is a long paper in which the authors attempt to show that any of the intestinal amoebae, most commonly *Endolimax nana* and *Entamoeba coli*, are liable to produce ill health. The commonest symptoms are tiredness and weakness associated with abdominal discomfort and diarrhoea. Treatment with carbarsone will get rid of the infection in a few days and at the same time there is an expression of relief in 44·1 per cent. of the cases. It is assumed that the amoebae were responsible for the symptoms in this percentage of the cases, while in the rest it is considered that some other cause was involved. In a discussion following the reading of the paper some speakers agreed with the authors while others thought that the large percentage of cases in which antiamoebic treatment did not produce relief disproved the authors' contentions. It is noted that the antiamoebic treatment was not the only curative measure adopted. Certain dietetic restrictions were made, while constipation, when it occurred, was dealt with. [For these reasons amongst many it would seem that a certain caution should be exercised before accepting the authors' conclusions.]

C. M. W.

HOOD (Marion). **Diarrhea caused by** *Dientamoeba fragilis*.—*Jl. Lab. & Clin. Med.* 1940. June. Vol. 25. No. 9. pp. 914–918. With 2 figs. [14 refs.]

Observations carried out in Chicago have shown the presence of *Dientamoeba fragilis* in the faeces of certain cases of diarrhoea associated with some abdominal distress. It is noted that emetine hydrochloride or other treatments employed for *Entamoeba histolytica* infections will also eradicate a *Dientamoeba fragilis* infection. It is concluded that the cases observed afford evidence of the pathogenicity of this amoeba.

C. M. W.

YAKIMOFF (W. L.). Un cas d'amibiase des porcs et la correlation entre l'amibiase de l'homme et des porcs. [**Correlation between Human and Porcine Amoebiasis.**]—*Jl. Microbiol., Epidémiol. et Immunobiol.* Moscow. 1940. No. 6. [In Russian pp. 65–68. [20 refs.] French summary (7 lines).]

A translation of the author's summary reads :—

The author has observed in a State farm that the pigs suffered extensively from disease. Some of the animals showed amoebae in large numbers and the author considers these to be *Entamoeba Debliecki-Nieschulz.*

In reviewing the available literature concerning correlation between human and porcine amoebiasis, the author concludes that this question is by no means settled. Nevertheless he records several cases of human dysentery which occurred along with the disease in the pigs.

C. W.

BROOKE (M. M.). **Supernucleate Cysts of** *Endamoeba coli.*—*Amer. Jl. Hyg.* 1940. Nov. Vol. 32. No. 3. Sect. C. pp. 100–111. With 5 figs. & 1 plate. [14 refs.]

It is well known that though the mature cyst of *Entamoeba coli* contains eight nuclei, under certain conditions, both in the intestine and in cultures, cysts with a larger number of nuclei may be encountered. In the present paper the author describes his observations on the cysts from a case of *E. coli* infection in which 33·7 per cent. of the mature cysts contained more than eight nuclei. These supernucleate cysts were generally larger than the ones with eight nuclei and had from ten to sixteen nuclei, except in three instances when 18, 22 and 30 were present. In supernucleate cysts the nuclei were variable in size. It is generally supposed that prior to encystment entamoebae divide to produce smaller precystic amoebae. It is suggested that if encystment occurs before this division has taken place there might be a tendency to the production of more than eight nuclei. *C. M. W.*

NUTTER (Paul B.), RODANICHE (Enid C.) & PALMER (Walter Lincoln). *Giardia lamblia* **Infection in Man.**—*Jl. Amer. Med. Assoc.* 1941. Apr. 12. Vol. 116. No. 15. pp. 1631–1632.

The authors have carried out a careful study of fourteen cases of *Giardia intestinalis* infection. In all cases there was persistent or intermittent diarrhoea. Other symptoms complained of were fatigue, weakness, abdominal pain with flatus, blood in the stools, insomnia, dizziness, nervousness and loss of weight. The blood of all the patients was found to be normal, except that of one with pernicious anaemia. Blood was found by benzidine technique in the stools of four, but this could be fully accounted for by co-existing disorders. Duodenal drainage showed vegetative forms of the flagellate in all but two of the cases. In these it must be assumed that the vegetative forms occurred elsewhere in the intestine. The microscopic appearance of the duodenal contents showed little, if any, abnormality. Although some observers have claimed that severe biliary symptoms may be associated with giardiasis this was not the case in the series studied. Treatment with atebrin (0·1 gm. three times a day for five days) will eradicate the parasite, the cysts disappearing from the stools in three days. In

only one of the cases was a second course necessary. The symptoms complained of often, but not invariably, disappear after treatment. In the present series the diarrhoea ceased in every case. [Though the series of cases observed is small it is clear that a very careful study of these has been made. The paper, in marked contrast to many publications which have been made on the subject, is a valuable contribution to our knowledge of the infection.] *C. M. W.*

BACILLARY DYSENTERY.

Précis of Abstracts in this Section.

Marshall and his co-workers (pp. 596, 597) describe the properties and pharmacological action of sulphanilylguanidine, a drug which is soluble in water but which is poorly absorbed from the gastrointestinal tract. The drug has been used for the treatment of acute bacillary dysentery in children and the authors give an account of 17 cases. The results in those cases in which treatment was commenced early were consistently good, but in those in which it was deferred the results were not uniform. A further series of 20 cases treated elsewhere is referred to ; in these the results were very good, improvement being in some instances dramatic. No definite toxic effects were observed. The authors give details of dosage. In comment it is noted that the infections concerned were with the Flexner and Sonne organisms ; it remains to be seen what effect the drug will have in Shiga infections. Lyon (p. 599) describes in more detail the series of patients referred to above. Ravenel and Smith (p. 600) report success in treatment with sulphapyridine and sulphathiazole, giving details of dosage and additional measures. Sulphanilamide is apparently ineffective.

Singh (p. 600) writes of the value of ispaghula, a preparation of the seeds of *Plantago ovata* or of *Spogel*, in the treatment of dysentery in India. *C. W.*

Marshall (E. K.), Jr., Bratton (A. Calvin), White (H. J.) & Litchfield (J. T.), Jr. **Sulfanilylguanidine : a Chemotherapeutic Agent for Intestinal Infections.**—*Bull. Johns Hopkins Hosp.* 1940. Vol. 67. pp. 163–188.

It has been found that several sulphanilamide derivatives, though water-soluble, are but poorly absorbed from the gastro-intestinal tract and thereby a new avenue of approach has been opened up to the chemotherapy of intestinal infections. Up to the present the use of intestinal antiseptics has depended upon low water solubility so as to avoid absorption ; in contradistinction the idea here expressed is in a drug which is purely water-soluble, therapeutically active, but is *not* absorbed from the intestinal tract. It is claimed that this departure presents a new principle in the use of the new bactericidal chemotherapeutic agents. The fundamental principle so involved is the achievement of a high concentration of the drug in the intestine contrasted with its low concentration in the blood and tissues—somewhat comparable with the concentration of sulphonamide derivatives in use as urinary antiseptics.

Sulfanilylguanidine was found to be the most highly bactericidal of the compounds studied. The authors have described a method for the preparation of N^4-acetylsulphanilylguanidine from which the drug is obtained by hydrolysis. The pure crystalline compound has a water solubility of 220 mgm. per 100 cc. and the solution is practically tasteless and has a *p*H of 6·9. The preparation and properties of the monochloride, dihydrochloride and picrate have been described.

The drug can be detected in blood, urine and cerebrospinal fluid by the colorometric methods employed for sulphanilamide derivatives. Dogs tolerate the maximum possible intravenous injection of 0·2 gm. per kilo. and it can be injected intraperitoneally in large doses dissolved in olive oil and is less toxic by this route than sulphapyridine. In rabbits it is converted into the *acetylate* and the acetylated derivative is deposited in the renal tubules causing diminished function. In mice absorption is slower than that of sulphapyridine by the mouth, but from the peritoneal cavity it is readily absorbed, penetrating all tissues rapidly with the exception of the brain, and it passes into the spinal fluid more slowly than either sulphanilamide or sulphapyridine. After intravenous injection it is excreted within 24 hours. From the small intestine it is probably more readily absorbed than from the large. Its effect against experimental mouse pneumonia is comparable with that of sulphapyridine, though somewhat less effective against experimental β-haemolytic streptococci, but *in vitro* tests with a number of bacterial species demonstrate that it is at least as effective as sulphanilamide, and the number of coliform organisms in the intestinal contents of mice is markedly reduced by placing them on a dietary containing 1 per cent. of this drug. *P. Manson-Bahr.*

MARSHALL (E. K.), Jr., BRATTON (Calvin), EDWARDS (Lydia B.) & WALKER (Ethel). **Sulfanilylguanidine in the Treatment of Acute Bacillary Dysentery in Children.**—*Bull. Johns Hopkins Hosp.* 1941. Jan. Vol. 68. No. 1. pp. 94–111.

Saturation of the intestinal contents with this drug can be obtained with a dosage that gives a low concentration in the blood, confirming deductions previously made from observations on experimental animals. The drug was prepared by the method described above. The monohydrate was employed, though figures in this paper for blood and stool concentrations refer to the anhydrous compound.

The technique of determination of the sulfanilylguanidine content of the stool is rather complicated ; it is gauged by a colorimetric process. A 5–10 gm. sample is taken from the total excreta, emulsified, filtered and 12 per cent. trichloracetic acid added.

Sulfanilylguanidine is soluble in water at body temperature to the extent of 200 mgm. per cent. A table is given of the concentration of the drug in the stools obtained with various dosage schedules which are sufficient for a saturated aqueous solution. In one particular case of ulcerative colitis, with ileostomy, material from the end of the small intestine contained the drug in concentrations greater than 200 mgm. per cent. In one case with a maintenance dose of 0·05 gm. per kilo. every four hours more than sufficient of the drug was present to ensure saturation with 1–4 stools per diem, whilst the blood concentration of the drug remained at a low level. Data are available on the concentration of sulfanilylguanidine in the blood with various dosage schedules. In children, for instance, with a maintenance dose

of 0·05 gm. per kilo. every four hours, determinations on 17 patients gave an average value of 1·91 mgm. per cent. for free sulfanilylguanidine and of 2·52 mgm. per cent. for the total drug; in this group the average acetylation of the drug in the blood was 24·2. It was noted that blood concentrations are higher in adults than in children with the same dosage, though there appears to be a slightly greater acetylation in adults than in children.

In the urine with a dosage of 0·05 gm. per kilo. every four hours, the average urinary excretion was 13 per cent. of the amount ingested every day and 31 per cent. was acetylated.

The clinical experience with the sulfanilylguanidine treatment of acute bacillary dysentery included 17 cases where the diagnosis was made certain by the recovery of the organism from the faeces. Treatment with the drug was commenced within twenty-four hours of admission as soon as the diagnosis of probable dysentery was made. Initial doses were 0·1 or 0·2 gm. per kilo. whilst maintenance doses varied from 0·1 gm. every 8–12 hours to 0·05 gm. per kilo. every four hours. In the case of vomiting, distension or severe dehydration, a period of preliminary starvation was instituted and parenteral fluids administered, as required, by the subcutaneous or intravenous routes. During the period of sulfanilylguanidine therapy, haemoglobin and leucocyte determinations were made every two days. Results of treatment initiated early in the disease differed strikingly from that later in the illness; in 7 children on or before the third day of the disease results were uniformly good. All were young—under five years of age—all had high fever prior to therapy; five had convulsions and six were seriously ill; but within 28 hours after treatment had commenced temperatures had fallen to 100·4°F. and the children subsequently remained afebrile. Some appeared well after only 24 hours' therapy and the diarrhoea was checked in from 1–3 days. In ten, treated late in the disease, from the 4–14th days, results were not uniform. In a similar number faeces culture became negative for dysentery organisms during treatment; in five, stools became negative on the last day of therapy and within two days of its discontinuance, but in one (Sonne infection) culture was positive after drug administration.

Several other children with chronic bacillary dysentery, typhoid fever, and one boy with chronic ulcerative colitis, showed no response to the drug.

To this series is added the testimony of Dr. G. M. Lyon of Huntingdon on the results of treatment of twenty cases controlled by a parallel series, using alternate cases [see below]. One case showed good therapeutic response, fourteen excellent; many recoveries were dramatic, and five only seemed to follow the general course of the untreated cases. The age of the patients is not stated.

No definite toxic effects were observed in the series of children, the vomiting which was noted being attributable to the disease and not to the drug. In twenty-five adults receiving the drug for a variety of conditions toxic reactions were suspected in three on rather uncertain grounds, one had unilateral conjunctivitis, a second mild haemolytic anaemia and a third slight fever. Most cases had a leucocytosis of 11,000–30,000 on admission to hospital, but the counts dropped to normal within three days and the drug did not appear to exert any deleterious effect on the leucocytes. In two cases there was a relative leucopenia from the commencement.

The following dosage programme is recommended for further trials of sulfanilylguanidine in bacillary dysentery :—

Initial dose 0·1 gm. per kilo. by mouth.

Maintenance dose 0·05 gm. per kilo. every four hours till the number of stools daily is less than four, subsequently 0·1 gm. per kilo. every eight hours for at least three days. The finely powdered drug is given in milk or water. It should not be continued for more than 14 days because of the possible danger of agranulocytosis.

For adults the dosage schedule is the same as for children except that the drug is given every 8 hours, 0·05 gm. per kilo. in place of 0·1 gm. per kilo.

[The data given in this paper, it will be noted, apply to Flexner and Sonne infections only. The results of this treatment on the more acute and toxic Shiga infections will be awaited with great interest. This review should be read in conjunction with the foregoing.]

P. M.-B.

Lyon (George M.). **Sulfanilylguanidine. Treatment of Acute Bacillary Dysentery.**—*U.S. Nav. Med. Bull.* 1941. Apr. Vol. 39. No. 2. pp. 278–293. With 2 figs.

In assessing the value of chemotherapy in acute bacillary dysentery it is important that cases included in study should be relatively similar in character and severity in order that a fair comparison can be made.

Twenty-three with acute bacillary dysentery were treated with sulfanilylguanidine and a similar number taken as controls ; alternate patients being treated.

Those that did not receive sulfanilylguanidine exhibited the characteristic clinical course with pyrexia, nausea, vomiting, bloody diarrhoea, abdominal cramps and tenesmus, sometimes prolapsus ani, thin purulent diarrhoea and loss of weight. In the third week there was a tendency to convalescence, intestinal indigestion and continued weakness. Of the twenty-three receiving sulfanilylguanidine five were not obviously benefited, whilst the remainder, eighteen, were strikingly improved. Many recoveries were dramatic: after institution of this drug therapy a fall of temperature and leucocyte count occurred within 24–48 hours, as well as closely parallel general clinical improvement and reduction in the number of stools. In 48 72 hours there was freedom from blood, pus and mucus in the stools. The drug is most efficacious when administered 3–4 days after onset of fever or diarrhoea. The percentage of failures may be higher when the drug is not given after the fifth day of illness, sometimes it seemed to be effective when given later.

Generally speaking the use of the drug is unaccompanied by toxic effects, and they appear to be less than that of related compounds (sulphapyridine and sulphathiazole). Of 23 patients only three showed tendency to nausea and vomiting, but these symptoms were quite as common in the control group. The patients were mostly children, but range in age was extreme, from 2 months to 75 years. Routine treatment consisted of the customary general measures, with good fluid balance, serum transfusions, intravenous dextrose, and, when indicated, a bland, high protein, low fat dietary.

Sulfanilylguanidine was given so that patients received 0·1 gm. per kilo. as initial dose and 0·05 gm. per kilo. every four hours as

maintenance dose. When the stools were less than five, frequency of administration was reduced so that the patient received 0·05 gm. every four hours as maintenance dose. Attempts were made to estimate the concentration of the drug in the blood. Concentration in the blood varied generally between 1·5 to 3·6 mgm. per cent., the highest observed was 5·2 mgm. per cent.

[A possible fallacy in this study is that the nature of the infecting organism was not ascertained and cases were, in many instances, the patients of fellow practitioners.] *P. M.-B.*

Ravenel (Samuel F.) & Smith (D. Lesesne), Sr. **The Chemotherapy of Bacillary Dysentery.**—*Southern Med. Jl.* 1941. May. Vol. 34. No. 5. pp. 504–510. With 10 charts. [13 refs.]

The incidence of bacillary dysentery in south-eastern United States is estimated at 20,000 cases a year with a fatality rate of about 5 per cent. It is considered that quantitative and qualitative replacement by intravenous glucose and blood transfusion continues to save many babies with dysentery and introduction of raw apple dietary and pectin may also have contributed something.

In spite of these advances dysentery continues to be a serious disease with prolonged exhausting course and high mortality, especially in small children.

The authors consider that a third epoch has now been reached with the introduction of sulphonamides. In 1938 and 1939 they used sulphanilamide in seven cases without demonstrable effect. Since July 1939 they substituted sulphapyridine, when the drug restored to health a female infant of 4 months who was dehydrated and comatose. Protocols of 20 cases are given, but unfortunately the nature of the infecting organism was not ascertained. Infants ranged in age from 2½ months to 2½ years. The action of the drug was seen in the cessation of pyrexia and the almost instant abatement of the diarrhoea.

One series was treated with sulphapyridine and another with sulphathiazole. The dosage varied from 1½ 2 grains per pound body-weight (220–286 mgm. per kilo.) for the first day and 1–1½ grains per pound each 24 hours thereafter; administration was stopped within 4–6 days in which time stools were normal. The tablets were crushed in a small quantity of water, milk or fruit juice and were given at intervals of 4–6 hours. Vomiting did not occur with sulphathiazole and was rare with sulphapyridine. Procedures ordinarily used to combat, or prevent, dehydration and shock were employed when indicated. The importance of early starvation and subsequent furnishing of adequate food and vitamins was not neglected.

P. M.-B.

Singh (B. H.). **A Simple Treatment of Dysenteries and Diarrhoeas.**—*Indian Med. Gaz.* 1940. Dec. Vol. 75. No. 12. pp. 733–734.

The author uses ispaghula (the seed of *Plantago ovata* or of *Spogel*) in the treatment of these conditions. The seeds are cleaned and a fresh decoction is prepared daily by boiling two drachms of the seeds in one pint of water for 10–15 minutes and then straining through cloth. This may be sweetened. The patient drinks 3 ounces every two hours and finishes the whole by the evening. It is soothing

and pleasant and acts probably by coating the inflamed bowel wall with a thin layer of mucilage. It is more effective in acute than in chronic cases. Calcium lactate in 10 grain doses may be given in addition if there is much blood in the stools, and if the latter are too frequent, the addition of 5–10 grains of alum to the decoction is advised. In amoebic dysentery emetine may be given at the same time.

The author claims good results from this method of treatment, but does not give figures. In an editorial comment it is stated that ispaghula is regularly used for chronic diarrhoea or dysentery in the Calcutta School of Tropical Medicine. *C. W.*

Hodge (E. H. Vere). **Modern Views of the Dysenteries and their Treatment.**—*Practitioner.* 1941. June. Vol. 146. No. 6. pp. 365–371. [18 refs.]

BERIBERI AND NUTRITIONAL OEDEMA.

Précis of Abstracts in this Section.

Pannekoek-Westenburg and van Veen (p.602), as a result of estimation of vitamin B_1 in the blood of healthy persons, of patients with nutritional oedema (in whom the values were found to be normal) and of patients with beriberi (in whom the values were not correlated with symptoms) conclude that at present this test is not of practical importance.

Meyers (p. 602) shows that aneurin possesses the properties of a true diuretic ; the excretion of aneurin in the urine after administration does not often give results which can be taken as indicating aneurin deficiency, but an increase in systolic blood pressure after administration of aneurin and adrenalin was marked in the beriberi patients so tested, but was not present in persons who had previously been on a diet rich in aneurin. This reaction appears to be a result of unbalanced vascular tone.

Shindo (p. 603) has studied the blood picture in infantile beriberi. He (p. 604) shows that in rats fed upon a beriberi-producing diet there is an increase in the blood platelet count and there appear pathological granules in the neutrophiles. Administration of vitamin B_1 restores these conditions to the normal.

Gutierrez (p. 604) has estimated the deterioration which occurs in preparations of tikitiki stored for long periods. He recommends that they should not be used later than one year after preparation, and that this date should be clearly marked on the containers.

de Ocampo and Cruz (p. 605) investigated the dark adaptation of patients with beriberi, and concludes that in most cases there is deficiency in vitamin A as well as in vitamin B.

Wirjoboedihardjo (p. 605) records nutritional oedema in Bodjonegoro ; this is not related to vitamin deficiency but to low albumin and cholesterol values in the blood resulting from a diet of poor quality. *C. W.*

PANNEKOEK-WESTENBURG (S. J. E.) & VAN VEEN (A. G.). Het vitamine B_1-gehalte van het bloed van gezonden en zieken. [**The Vitamin B_1 Content of the Blood of Healthy and Sick Persons.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. July 23. Vol. 80. No. 30 pp. 1774–1784. With 1 chart. [21 refs.] English summary.

"1. Of 390 blood samples of healthy and sick people the quantity of aneurin present was determined by means of Schopfer's Phycomyces test as modified by Meiklejohn.

"2. The aneurin values (not corrected with Sinclair's factor), found in the blood of 90 normal natives, which were on an average $9 \pm 2\gamma$ per 100 cc. of blood, agree with those mentioned in European and American literature. As the limit of B_1 deficiency we assumed a value of $5{\cdot}5\gamma$. In 6 out of these 90 persons the aneurin content of the blood was $5{\cdot}5\gamma$ or less.

"3. The B_1 levels in the blood of 165 nutritional oedema cases on the whole agreed with those of normal persons. There is probably no relation between the nutritional oedema observed here and the vitamin B_1 level of the organism. Only in one group of 22 persons the number of low values was large, viz. 13. A possible explanation is to be found in the fact that these cases had extreme anaemia with low blood cell volumes.

"4. In 19 patients with clinically evident beriberi very divergent aneurin values were found; 9 of them were definitely low, but normal aneurin contents also occurred amongst them even in serious cases. This may partly be explained by the fact that these out-patients may have had B_1-rich food and even B_1 tabloids before treatment began, as the cause of beriberi is well-known by many natives. Since the organism cannot store up much vitamin B_1 the body and the blood may soon be 'saturated,' while the clinical symptoms of beriberi still exist.

"5. All but two of 19 polyneuritis patients of various origin had a normal B_1 level. The two low values were one case of lues and one of alcohol-polyneuritis.

"6. The aneurin content of 10 tabes dorsalis patients was normal. This number is however too low for conclusions.

"7. From the above it will appear that the determination of aneurin in blood is as yet of no great practical importance. No conclusions as to the presence of a B_1 deficiency may be drawn merely from the aneurin level of the blood; the cell volume should also be taken into account."

MEYERS (F. M.). Clinische onderzoekingen in verband met beri-beri: III. Over het z.g. "subclinische" aneurine (vitamine B_1) tekort. [**The So-called Subclinical Deficiency of Aneurin (Vitamin B_1).**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. July 16. Vol. 80. No. 29. pp. 1727–1746. With 2 graphs. [38 refs.] English summary.

"In a preliminary remark it is pointed out that descriptions of subclinical aneurin (vitamin B_1) deficiencies from the temperate parts of the world show a much wider range of symptoms than those of the tropics. It is believed that this difference in symptoms arises from different conditions of disease. In the Netherlands East Indies at

least, aneurin deficiencies are relatively uncomplicated and chiefly of exogenous origin. In Europe and in the United States, these subclinical deficiencies are often conditioned by alcoholism and chronic diseases of the intestinal tract and are mixed furthermore with pellagra in its forme fruste.

" In a number of cases of healthy Javanese estate-labourers, the excretion of aneurin in the urine has been investigated before and after subcutaneous test doses. At the same time attention has been paid to the diuretic effect of aneurin and to its influence on the increase of blood pressure after epinephrine. The findings could be compared with those of 3 healthy ' prepared ' persons who had received a diet rich in aneurin and with those of 3 cases of mild beri-beri.

" In the healthy individuals the daily excretion of aneurin was found to be from 0–63 micro g., with an excretion after test doses of 2–50 per cent. (in most cases : 10–30 per cent.). One healthy ' prepared ' person, however, showed excretion values of the same order as those of the patients with beri-beri.

" In 9 out of 14 healthy persons, a definite diuretic influence of the test doses could be established. There was no clear correlation with the aneurin excretion values. Aneurin has properties of a true diuretic.

" In 3 out of 8 healthy individuals, the increase of systolic blood pressure after epinephrine became much stronger after the test doses with aneurin had been given.

" The same occurred in the cases of beri-beri, but in none of the 3 ' prepared ' individuals. Thus this vascular reaction proved to be a valuable means in establishing conditions of aneurin deficiency where other means had failed ; but no definite correlation could be detected with the excretion of aneurin in the urine. The reaction seems to be a consequence of an unbalanced vascular tonus : with repeated injections of epinephrine and before the test doses had yet been given, the rise in blood pressure became much stronger as was the case in the persons with a negative vascular reaction.

" The excretion of aneurin in the urine alone, often does not seem to produce figures that are sufficiently unequivocal to judge, whether in individual cases a condition of deficiency is present or not."

Shindo (Masayuki). **Change of Blood Picture of Infantile Beriberi, Infantile Preberiberi (Sato) and Infantile B-avitaminotic Dyspepsia (Sato) on an Administration of Vitamin B.**—*Tohoku Jl. Experim. Med.* 1940. July 5. Vol. 38. No. 5. pp. 403–413. [23 refs.]

The haematological findings are tabulated of 23 breast-fed infants diagnosed as cases of infantile beriberi, infantile preberiberi or B-avitaminosis.

The author concludes that the blood pictures are characterized by anaemia, hypohaemoglobinaemia, thrombocytosis, neutropenia with an increase in pathological granules and a nuclear shift to the right, lymphocytosis and eosinophilia. [It seems doubtful, however, whether all these conclusions are justified, as many of the author's figures do not depart significantly from those found in normal infants.]

In 6 of the cases further examinations were made after vitamin B_1 had been administered, and a return of the blood pictures to normal was noted. The actual figures, however, are not given.

L. J. Davis.

SHINDO (Masayuki). **An Experimental Study on Blood Platelets and Pathological Granules of Neutrophiles in Rice-Diseased and B_1-avitaminotic Rats ; and Change of Blood Platelets on an Administration of Vitamin B_1.**—*Tohoku Jl. Experim. Med.* 1940. June 5. Vol. 38. No. 4. pp. 380–402. With 4 figs. [28 refs.]

" 1. White rats fed on thoroughly washed polished rice or on diet free from vitamin B_1 show an increase of blood platelet count.

" 2. But when polished rice or B_1-free diet is long continued or when animals draw near death or are in the paralytic stage, the count decreases.

" 3. As to classification of blood platelets, the sum of spindle-shaped and small platelets show an increase when total count begins to increase or return to normal, and large platelets show an increase in the more advanced stage of B_1-avitaminosis.

" 4. Vitamin B_1 makes the increased blood platelet count smaller and renders the abnormal distribution of different platelets normal.

" 5. ' Neutrophiles with pathological granules ' already show an increase, though in a slight degree, then platelet count begins to increase.

" 6. Red cell count does not decrease in the terminal stage of B_1-avitaminosis, but shows an increase when platelets reach the maximal count in most cases.

" 7. There is, as far as platelet count and pathological granules is concerned, no essential difference between the rice disease and B_1-avitaminosis of rats.

Conclusions.

" From these studies it may be concluded that in B_1-avitaminosis and rice disease, blood platelets and the percentage of ' neutrophiles with pathological granules ' will become larger except in the terminal stage, and that vitamin B_1 will make the increased count smaller and render the abnormal distribution of different platelets normal."

GUTIERREZ (M.). **The Stability of the Vitamin B_1 Content of Tikitiki Extract and a Syrup Preparation of Vitamin B_1.**—*Acta Med. Philippina.* 1940. Oct.–Dec. Vol. 2. No. 2. pp. 189–198. With 1 fig. [16 refs.]

The preparations examined were a sample of tikitiki extract manufactured by the Philippine University College of Pharmacy and a sample of Benerva Syrup, a preparation of vitamin B_1. They had been previously assayed by the rat-growth method, and as a reference standard that of the League of Nations in 1931, the fuller's earth adsorbate. The same method was used in the re-assay, but the reference standard was that of the U.S.P. which has the same potency as that of the League previously used. The tikitiki extract was administered undiluted in daily doses (except on Sundays) of 0·05 ml. and the syrup so diluted as to contain in each daily dose of 0·1 ml. 9·8 mgm. of undiluted syrup.

The tikitiki assayed in May 1939 had given a potency of 10 I.U. per gramme ; after 18 months' storage this had fallen to 5 I.U. The Benerva Syrup had given 51 I.U. per gramme and a year later had fallen to 20 I.U., deteriorations of 50 and 60 per cent. respectively.

The author recommends that expiration dates should be fixed by manufacturers to their products after which they may not be sold, as they become almost valueless as sources of vitamins. For tikitiki this date should be one year after that of manufacture. Further study is to be undertaken to determine the cause of the deterioration ; fermentation and changes in *p*H have been excluded. *H. H. S.*

DE OCAMPO (Germiniano) & CRUZ (Jose N.). **Dark Adaptation in Adult Beriberi.**—*Acta Med. Philippina.* 1940. Oct.–Dec. Vol. 2. No. 2. pp. 175–188. With 2 graphs. [16 refs.]

This study was undertaken to determine whether beriberi patients have a deficiency in vitamin A as well as in vitamin B_1. The instrument used was Model D biophotometer, made by the Frober-Fayber Co. of Cleveland, Ohio. By this is determined " the amount of light necessary for the subject to see some standard objects after exposing him to a more or less constant amount of bright light, as well as the minimum quantity of light necessary after ten minutes of dark adaptation." The length of the period for recovery is important. With most instruments the light is constant and the time element is measured ; with the model D the time element is constant and the intensity of light is measured.

Twenty-five patients were investigated ; three are described in detail as representative cases. Of the 25 seven were males and eighteen females ; ages ranged between 18 and 45 years. Care was taken to exclude any with organic eye disease which might reduce dark adaptation ; and in the analysis 23 only are considered, the other two having subnormal vision.

Of the 23 " one-fifth had more or less normal dark adaptation " ; [" one-fifth " would be four or five, but in a table the number is given as three]. The conclusions are expressed [badly] in percentages.

" Forty per cent. of those remaining " [one-fifth being 4 or 5, 40 per cent. of the remainder might be 7 or 8] is shown in a table to be eight and these had slightly impaired adaptation ; " thirty per cent. (*i.e.* six) had moderate and the same number marked impairment of adaptation." In other words adult beriberi patients have a deficiency in vitamin A, and it may be that corneal lesions noted in some beriberi patients are the result of this avitaminosis A. Five only complained of night blindness, and, as FELDMAN has observed (*Arch. Ophthalm.*, 1939, Vol. 22, p. 595) there is " no constant and direct relationship between the symptoms of night blindness and dark adaptation."

H. H. S.

WIRJOBOEDIHARDJO (M. Ismangil). Ondervoedingsoedeem in Bodjonegoro. [**Nutritional Oedema in Bodjonegoro.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. Aug. 27. Vol. 80. No. 35. pp. 2063–2082. With 12 figs. on 3 plates. [13 refs.] English summary.

" 1. From the local knowledge of the region, in which the poor inhabitants of Bodjonegoro live, their food, their clinical condition, the chemistry of their blood and the therapeutic effect of better nutrition, we may conclude that there existed *underfeeding-oedema* at Bodjonegoro.

"2. We explain this oedema by the diminution of the albumin concentration, resulting in a diminution of the oncotic pressure, combined with the decrease of the cholesterol concentration in the serum.

"3. The vitamins are not of any importance in causing the oedema.

"4. This oedema soon disappears when substantial food and rest is given to the patient, except in very serious cases."

EPIDEMIC DROPSY.

Précis of Abstracts in this Section.

Lal and Das Gupta (p. 606) report an outbreak of epidemic dropsy which adds confirmation to the argemone oil theory of causation. Nath (p. 607) reports an outbreak in which the association with the oil of *Argemone mexicana* is very clear. Hart (p. 607) from New South Wales reports that in fowls fed on a diet containing argemone seed there developed a condition closely akin to human epidemic dropsy. Lal *et al.* (p. 607) record the appearances caused in cats and rats fed on a diet containing argemone oil; dropsy could not be produced, but in rats the skin changes resembled those seen in human epidemic dropsy.

Palit *et al.* (p. 608), however, consider that epidemic dropsy is not a single disease, but that the term covers a number of conditions. They hold that the argemone oil theory has been too readily accepted.

Pasricha *et al.* (p. 608) found increased sedimentation rate in epidemic dropsy, and that this increase may take place before clinical symptoms develop. *C. W.*

Lal (R. B.) & Das Gupta (A. C.). **Investigations into the Epidemiology of Epidemic Dropsy. Part X. A Note on an Outbreak of Epidemic Dropsy associated with the Use of Mustard Oil Pressed from Seeds Adulterated with Seeds of** *Argemone mexicana*.—*Indian Jl. Med. Res.* 1941. Jan. Vol. 29. No. 1. pp. 157–165. With 1 sketch map & 4 figs. on 1 plate.

Another typical instance of an outbreak of epidemic dropsy adding confirmation to the argemone oil theory of causation. The cases occurred in a remote village in Northern Bengal where no cases had been previously recorded. The community consisted of 89 persons belonging to 11 families, and the number attacked was 24 in five families, all the members of all the five families except one who had been away during the outbreak. All the villagers intermingled freely, but the source of their supply of rice was individual. Mustard oil was consumed by all, but the five families affected obtained it from a common source, the other families bought theirs elsewhere. The oil used by the former contained more than 5·7 per cent. of argemone oil and it was used, up to ¾ oz. per head per day, for at least ten days before the beginning of the outbreak; each, it was estimated, had consumed at least 25 mgm. of the reacting substance of the oil, and the amount may have been 50 mgm. or more. The disease was of a severe type and three patients died. No one was attacked who did not consume oil from this source. *H. H. S.*

Bengal Public Health Journal. 1940. Dec. Vol. 2. Nos. 2 & 3. p. 98.—**A Report on the Occurrence of Epidemic Dropsy in a Village by Hari Prosad Nath, Sanitary Inspector, Balurghat, Dinajpur.**

The author records briefly an outbreak of epidemic dropsy in which 23 persons living in 10 houses were attacked. Two of them died. The history is very clear. A village manufacturer of mustard oil collected katagar seeds (*Argemone mexicana*), mixed them in a proportion of one part to two of mustard seed, extracted the oil from the mixture and sold it in the village. Five other families living adjacent to those attacked did not use this oil and were not affected. [The author does not state how much was used, nor for what length of time before symptoms appeared.] *H. H. S.*

Hart (L.). **The Toxicity of Seeds of *Argemone mexicana* for Fowls.**—*Australian Vet. Jl.* 1941. Apr. Vol. 17. No. 2. pp. 69–71.

Mexican poppy, *Argemone mexicana*, is a common weed in New South Wales, and the seed is mixed in the food of fowls. Fowls were reported to be dying after suffering from diarrhoea and a peculiar high-stepping walk, and at autopsy the abdominal cavity was found to contain much fluid and the subcutaneous tissue was oedematous, as were the lungs ; the intestines were congested.

Experiments were carried out and it was found that some 25 grammes of the seed mixed with 5–6 times this amount of wheat over a period of 9–12 days were needed to produce symptoms : darkening of the tips of the comb, difficulty in walking, inability to stand, oedema of wattles and subcutaneous tissue. Post mortem, the oedema was marked, with congested intestine, and catarrhal enteritis. Death occurred in 4 weeks, a little less or more (26–31 days), but if the seed was removed from the food in time the bird would slowly return to health.

[Readers will notice the similarity between these symptoms and those of epidemic dropsy in man—a fact adding further confirmation of the argemone toxin theory of the causation of this disease, see this *Bulletin*, 1939, Vol. 36, pp. 909, 910; 1940, Vol. 37, pp. 748–751; 1941, Vol. 38, p. 288.] *H. H. S.*

Lal (R. B.), Chatterji (S. R.) & Agarwala (S. P.). **Investigations into the Epidemiology of Epidemic Dropsy. Part XI. Biological Test of Specific Toxin in Samples of Oil.**—*Indian Jl. Med. Res.* 1941. Jan. Vol. 29. No. 1. pp. 167–193. With 11 graphs & 12 figs. on 3 plates.

The authors in their search for biological tests used rats, cats, guineapigs and pigs. In none of these were they able to produce the clinical signs of epidemic dropsy. They, therefore, had to rely on such criteria as time to death, loss of weight and histological changes, especially of the skin. The animals were fed on pure mustard oil, on olive oil, on pure argemone oil, on 5 per cent. argemone oil, and on Rangpur oil which is known to be toxic. Cats and rats showed depression of growth greater with the argemone oil than with pure mustard oil added to the basic diet and in rats the skin changes resembled those found in patients with epidemic dropsy. Neither guineapigs nor pigs appeared to be suitable for the biological test.

H. H. S.

PALIT (C. C.), BASU (S. N.) & VARMA (V. L.). **Epidemic Dropsy and Mustard Oil.**—*Jl. Indian Med. Assoc.* 1941. Mar. Vol. 10. No. 6. pp. 251–262. With 5 charts. [23 refs.]

From a number of experiments on pigeons and chemical analyses of foods and biochemical tests the authors have been led to conclude that epidemic dropsy is not a single disease, but a term which in reality comprises a group of conditions. They advocate further intensive research on three lines: (*a*) the possibility of an infective agent being responsible, (*b*) the action of some chemical poison, (*c*) a metabolic deficiency. They think that the argemone oil theory has been too readily accepted. *H. H. S.*

PASRICHA (C. L.), MALIK (K. S.) & LAL (S.). **Sedimentation Rate of Red Blood Cells in Epidemic Dropsy.**—*Indian Med. Gaz.* 1941. Jan. Vol. 76. No. 1. pp. 34–37. With 1 graph.

The authors estimated the sedimentation rate of red corpuscles in 74 patients suffering from epidemic dropsy and in 8 others presenting similar symptoms after food cooked in mustard oil which had been incriminated as causing disease. They estimated also the cell-volume and haemoglobin percentage. They found that the sedimentation rate was increased in epidemic dropsy in every case and the rate-increase went *pari passu* with the degree of severity, and the higher the rate the graver the prognosis. It appeared from the evidence that this increase begins before clinical symptoms develop; it is, therefore, of epidemiological value. In 20 cases of the disease the fibrin-nitrogen content was estimated, and this and the cell volume and the sedimentation rate were found to be interrelated. "An increase of fibrin leads to an increase in the sedimentation rate provided the cell volume is constant. An increase of cell volume decreases the sedimentation rate provided the fibrin content is constant." *H. H. S.*

REVIEWS AND NOTICES.

WAR OFFICE. **Memoranda on Medical Diseases in Tropical and Sub-Tropical Areas 1941.** Sixth Edition.—282 pp. With 108 figs. & 1 double plate. 1941. London: H.M.S.O. [3*s.* 6*d.*]

It is eleven years since the fifth edition of this book was published, and during this period there have been advances in the knowledge of many branches of tropical medicine. In the subjects with which the book deals, most of these advances are recorded, and a great deal of trouble has evidently been taken to bring it up to date and yet to avoid discursiveness. In his preface Lieutenant-General Sir W. P. MACARTHUR points out that it is not a substitute for any of the well-known treatises on tropical medicine and that, as the memoranda are intended for use in the field, the volume is not claimed to cover the whole range of tropical medicine.

The format of the previous edition is maintained, the type used is smaller and the book is shorter by 30 pages. The index has been expanded, with considerable improvement. The subject matter is dealt with, as before, in alphabetical arrangement, which is unsatisfactory from the point of view of continuity and classification, and is not particularly helpful in rapidly looking up any subject, especially as there are no running titles at the page heads.

A chapter on cysticercosis has been added, and contains a full account of the condition, with emphasis on the importance of bearing it in mind in the consideration of epilepsy in soldiers from India. The chapter on fevers in the east has been omitted from this edition.

The points on which criticism is possible are not of great importance. In the prevention of malaria more emphasis might have been laid on the value of fumigants for buildings, recent work in India, Africa and Holland having shown that this is by no means a negligible procedure. It is not impossible that Army Medical Officers may be called upon to treat epidemics of cholera among refugees; if this happens, the rough and ready, but effective, method of treatment lately in use in China may be worth bearing in mind; it is essentially a mass intravenous infusion of normal saline. The importance of eliminating pyrogenic substances from distilled water used in the large injections necessary in cholera has been recently stressed and would bear mention.

On pages 86 and 87 the word used in the captions should surely be "atypical"—not "a typical."

The common causes of diarrhoea in the East are stated to be "exposure to chill, and irritation of the bowel by sand and dust or by coarse and unsuitable food," but in the opinion of the reviewer it is much more likely that bacterial infection is responsible. There has indeed been some recent correspondence on this subject in a medical journal and the majority of writers favour the bacterial origin. The classical treatment of bacillary dysentery is advised, but there is now reason to think that drugs of the sulphonamide group may eventually provide the treatment of choice, though the work on which this view is based was probably not reported when the book was being prepared.

The author has perhaps been over cautious in discussing the transmission of leishmaniasis; there is now little doubt that the sandfly is the usual agent. In the diagnosis of kala azar, gland puncture should be mentioned. For the prevention of malaria the author summarizes, in wise words, the general opinion of the value of drug prophylaxis, which cannot be discarded with impunity under war conditions; no undue claims are made, but its value in staving off clinical attacks is recognized. In these days when blood transfusion plays so great a part in war surgery it would have been well to mention the possibility of transmitting malaria with the donor blood, even if parasites cannot be found in it, or of reactivating latent malaria in the recipient.

The author mentions plague as a disease of rats, but does not refer to sylvatic plague, which is a subject of increasing importance in Africa and doubtless in other countries in which the Army may be called upon to operate; there are several foci in East Africa. He makes mention, however, of recent encouraging work on the sulphonamide treatment of plague.

In the treatment of schistosomiasis Fouadin and Anthiomaline receive no mention; it is probably true that they are not so effective as tartar emetic, but as alternatives they have their place. In

prevention a reference to SPROULE's recent work on the destruction of cercariae by chlorination in Army water carts would have been timely [see this *Bulletin*, 1940, Vol. 37, p. 148]. The chemotherapy of sleeping sickness and of kala azar has lately been strengthened by YORKE's work on 4 : 4′-diamidino stilbene, which appears to be most satisfactory in the refractory kala azar of the Sudan. In the treatment of sprue, nicotinic acid is probably of greater importance than the author indicates.

There is a good account of trench fever and of the typhus group ; it would be well to emphasize that, in the Weil-Felix reaction, only agglutinations of the *O* variants of *Proteus X19* and *XK* are valid.

These are the criticisms which may be made ; they are of minor details only. Against them may be set the virtues of clarity and conciseness and the authoritative setting out of known facts in order. The work is not over-dogmatic, as it might have been, and discussion of debatable subjects is not avoided. For its declared purpose the book is excellent. *C. W.*

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BULLETIN OF WAR MEDICINE.

The attention of readers of the *Tropical Diseases Bulletin* is drawn to a new publication entitled the *Bulletin of War Medicine*, issued by the Medical Research Council, edited and prepared by the staff of the Bureau of Hygiene and Tropical Diseases, and published by H.M. Stationery Office.

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